IJBPAS, March, 2023, 12(3): 1099-1108

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

NASAL GEL AS PROMISING DRUG DELIVERY SYSTEM: AN OVERVIEW

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Received 14th April 2022; Revised 11th May 2022; Accepted 1st Aug. 2022; Available online 1st March 2023

https://doi.org/10.31032/IJBPAS/2023/12.3.6936

ABSTRACT

For thousands of years, nasal drug delivery has been practiced and has brought a new lease on life. Nose cavity were considered as complementary path for systemic accessibility of medicament those have limitation to administer it intravenously. This is because of porous endothelial membrane, elevated blood flow, greater surface area, more penetration of certain medicaments in the nose membrane, and ameliorates the patient's compliance with the quick absorption of medicaments via this membrane. Also it confers quick onset of action, enhanced patient acceptance and satisfaction, sustained activity when correlate with various system of drug delivery. In a nasal drug delivery system, formulations such as nasal gel achieved recent attention in a pharmaceutical domain possess multitudinous effects of other nasal formulations like solids, liquids and sprays. The formulations of nasal gel are easy to prepare, more apparently acceptable as it offers quick onset of action, avoids first pass metabolism, minimum risk of side effects, elevated residence time, and enhanced patient compliance. This review sets out to discuss benefits, drawbacks, method of preparation, different additives used in nasal gel and evaluation parameters of nasal gel.

Keywords: Bioavailability, first pass metabolism, nasal gel, evaluation, etc

INTRODUCTION:

Oral administration is an utmost preferential path of drug incorporation, but it has disadvantages such as chemical and enzymatic deterioration of drugs in GI

region, inadequate mucosal penetrability, and first-pass metabolism in liver. Although the parenteral routes impart good bioavailability, it also has certain drawbacks, such as pain upon insertion and poor patient compliance. Intranasal system of drug administration is a recent progression in the drug administration technology. It offers various benefits over conventional drug delivery systems **[1, 2, 3]**.

Drug deliver for local and systemic effect via nose has been esteemed as pivotal and voguish way to enhance bioavailability. Nasal mucosa was considered to be a potential administrative path to attain a faster and superior absorption as it penetrable to more compounds than the GI region because of absence of pancreatic and enzymatic action, neutral pH of the nose mucous and minimum dilutions by GI contents. In progressive years, many drugs have been shown to gain the best systemic bioavailability via nose than by oral. Nose therapy was a distinguished pattern of remedy in the Ayurvedic system of Indian medicine, and it is also called **"NASAYA KARMA"**. Incorporation of drugs without needle enhanced patient compliance with choice of self-medication **[4, 5]**.

The internal structure of nasal cavity and its connection to other organs shown in **Figure 1** and **Figure 2** respectively **[6, 7]**.

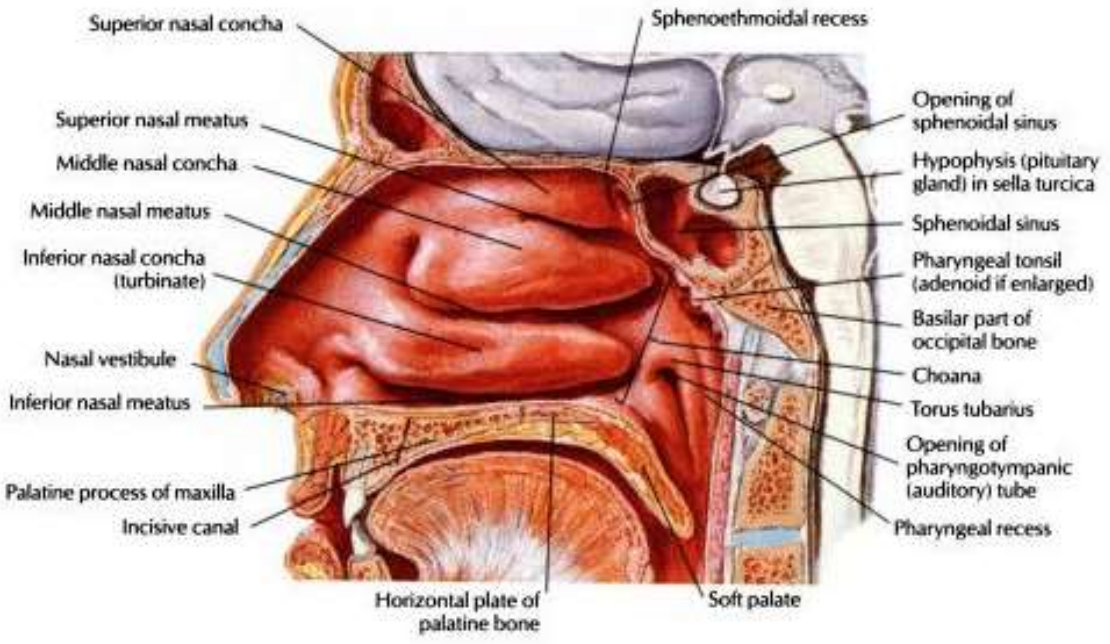


Figure 1: Internal structure of nasal cavity

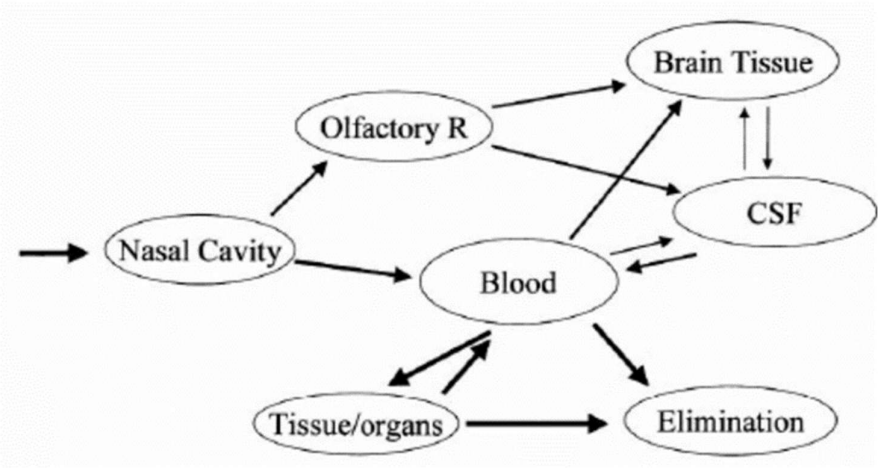


Figure 2: Connections of nasal cavity to other organs

Nasal gels are concentrated solutions or suspensions with high viscosity. There was no interest in this system until the recent advancement of precise dosing devices. Benefits of nasal gels include minimization of post nasal drips because of high viscosity, minimization of anterior drug leakage, minimization of irritation through the use of soothing or emollient excipients, and targeted mucosal delivery of superior absorption. The deposition of the gel in the nasal cavity depends on the method of administration, since the formulation is not well distributed due to its viscosity. It only occupies a compact distribution area in the nasal cavity where it is installed directly without any special application procedures. Very recently the first nasal gels containing vitamin B 12 appeared on the market for systemic treatment **[8]**.

The Devices that used for nasal delivery are shown in **Figure 3 [9]**.

Figure 3: Devices used in nasal delivery

BENEFITS: [10, 11]

- Achieved rapid absorption of the drug and quick onset of action.
- Greater bioavailability.
- Quick onset of therapeutic activity.
- First-pass metabolism is avoided.
- Prevention of gastrointestinal irritation.

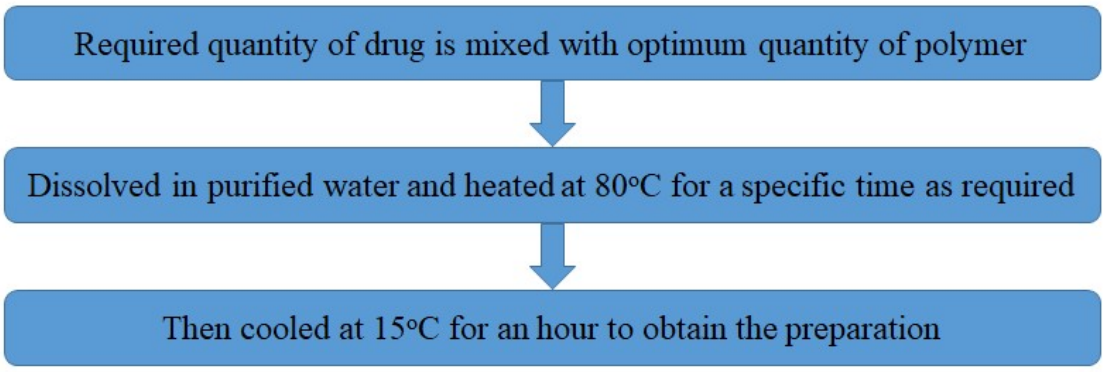
- Risk of overdose is prevented.
- Unobstructive, thereby reducing the problem of communicable disease transmission.
- Comfort and self-medication
- Patient compliance has improved.
- Deterioration of drug in GI region is prevented.
- Suitable for the medicaments which are unable to be absorbed by the oral route.
- Drugs with poor gastrointestinal stability are administered nasally.
- Polar compounds with poor oral absorption may be particularly suitable for this route of delivery.
- Suitable for the polar compound having low absorption by oral route.

a) method- I:

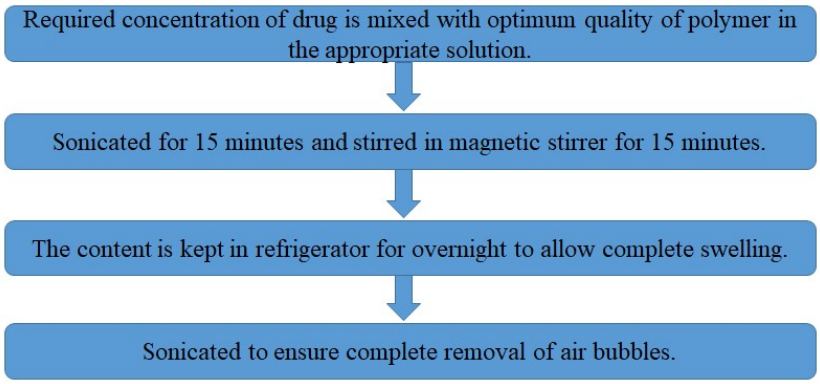
DRAWBACKS: [12, 13]

- The mucociliary eviction decreases the residence time of the drug.
- Residence time of drug reduces because of mucocillial clearance.
- Not all drugs are covered.
- Large capacity (25-200 ml) is required based on the water solubility of the drug.
- Mechanical loss of formulation to other parts of the respiratory tracts, such as lungs it may occur because of inappropriate dosing technique.
- There are certain drugs that can cause nasal irritation.
- The nose opening has lesser area for absorption as compare to GI region.

METHOD OF PREPARATION:



b) method- II:



ADDITIVES USED: [14, 15, 16]

1] **Thickening Agents:** Thickening agents offer the optimum viscosity to preparation, which helps in the prolonged effect of nasal gel preparation such as Hydroxypropyl cellulose.

2] **Solubilizers:** Solubilizers are the agents used in nasal gel to provide the solubility of drugs. They may be in the form of co-solvents such as glycerol, required quantity of alcohol. Surfactants and Cyclodextrins can also be used as solubilizing agents.

3] **Preservative:** A number of preservatives are used in nasal gel formulations to prevent microbial growth, such as Ethylenediaminetetraacetic acid (EDTA), Parabens, Benzalkonium chloride, and Phenylethyl alcohol.

4] **Anti-oxidants:** Anti-oxidants such as Sodium bisulfite, Sodium pyrosulfite, Dibutylhydroxytoluene, and tocopherol are needed to prevent oxidation of nasal gel formulations. In general, antioxidants do not affect the absorption of drugs and ensure the stability of the formulation.

5] **Humectants:** The mucous membrane affected by some allergic and chronic diseases such as crusts, dryness and irritation can be caused by preservatives/ anti-oxidants when used in large amounts. Intranasal moisture is crucial to prevent dehydration and humectant should be used in gel- based nasal products. Humectant prevent irritation, but do not interfere with drug absorption. These are Sorbitol, Glycerine, and Mannitol.

6] **Penetration enhancers:** The penetration enhancer is used to enhance the absorption potential of the drug. Generally they are used when nasal gel faces the difficulty to achieve the required absorption.

Commonly Alpha-cyclodextrin, Beta-cyclodextrin, Gamma-cyclodextrin, Methyl-cyclodextrin, and Hydroxyl-cyclodextrin are used. However, in many studies, it was found that beta cyclodextrin is most important because it provides more absorption potential in the nasal gel preparations. The penetration enhancers can be used when the drug has low membrane penetration, big molecular weight, deficits of affinity towards lipid, and enzyme cleavage by aminopeptidase.

Penetration enhancers work by mechanisms given below:

- Suppression of enzymatic action.
- By decreasing mucous consistency or flexibility.
- Reducing mucocillial eviction
- By opening of stiff jointure.

EVALUATION PARAMETERS:

1] Clarity:

Preparations were examined clearly against a dark and white background and the purity of the preparations were rated in this manner:

- Turbid - +
- Clear - ++
- Very clear - +++

2] pH:

Each 1 ml gel sample equal to the corresponding amount of drug was moved to a 10 ml volumetric flask and diluted with DW. The pH of resultant solution was measured by use of a pre-calibrated digital pH meter prior to measurement. The pH of the preparations should be within the standard physiologic pH range of the nose mucous membrane (4.5-6.5) **[17-20]**.

3] Rheological study:

The viscosity of the formulations were analyzed by making use of apparatus called viscometer (Brookfield). The evaluating system used was the C-25, which is typically utilize for more viscous fluids such as gum, mucus, and polymer dispersion. Evident viscosities were noted at various rotations in between 10-100 RPM at room temperature. **[21]**

4] Drug content:

The drug content of each preparation is measured by diluting 1 ml of the formulation to 100 ml with an appropriate solvent and shaking intensely. 1 ml was remove from the solution and then diluted to 25 ml with the same solvent. The absorbance of the solution was determined spectrophotometrically at a specific wavelength. The drug content (%) was calculated by use of given equation: **[19, 22]**.

Drug content (%) = Drug concentration (sample solution) / Equivalent concentration (drug taken) * 100

5] Gel strength:

An appropriate amount of prepared gel sample was placed in a 100 ml measuring cylinder. Then, a 35 g weight was positioned on a disc have wideness of 2.3 cm, a distance of 0.4 cm from the sidewall of the cylinder, and a thickness of 0.5 cm, and this disc was positioned on the gel. Gel strength was measure as the time (in second) needed to move the disc downside (5 cm) through the gel. The strength of the gel is associated with molecular weight, degree of crosslinking, etc. If lowering of the device through the gel took longer than 5 minutes, additional weight was positioned on top of the device and the gel strength was illustrated as the minimum weight that pressed down the device (5 cm) through the gel **[23]**.

6] Spreadability test:

Spreadability was calculated using apparatus consisting of wooden plank with scales and pair of glass slides with two pans on either side hanged on pulley. An extra sample was placed between the two slides, and a 100 g weight was kept on the slide for 5 minutes to press the sample to a uniform size. Added a load (250 g) to the pan. The time (in second) needed for detachment of two slides was considered as a measure of spreadability **[24]**.

S = m* l / t

Whereas,

m – Weight attached to top slide

l – Length of slide

7] Diffusion study:

Diffusion studies for numerous preparations were performed using Franz diffusion cells. A dialysis or egg membrane was used as the diffusion membrane. The membrane was saturated in a specific solvent for 24 Hrs before the experiment. The receptor chamber was filled with the required amount of solvent and the membrane was placed over the cell. The gel corresponding to the appropriate amount of drug was placed in the donor chamber. The temperature was maintained at 32-34 °C using a circulating water bath. Samples of 1 ml were taken at specific time intervals, refilled with an equal amount of fresh solvent to maintain sink condition, filtered, and finally the absorbance of the drug was determined spectrophotometrically at specific wavelength **[25]**.

CONCLUSION:

From this article we concluded that, in the past few years the nasal cavity has become one of the providential and conceivably adaptable route for drug delivery. Intranasal drug delivery system provides various types of formulations such as solution, spray, powder, but nasal gel preparations have been more effective in the term of increased residence time, increased bioavailability, and quick onset of action. Additives used in the nasal gel preparation are also crucial because these provides the

safety of formulations such as prevents the microbial attack by using preservatives, increased solubility by using solubilizing agent, prevent the dryness by humectants, reduced the risk of oxidation by using antioxidants, enhanced the viscosity by using viscofying agent. It is intimately proposed that this review will guide to comprehend and further to advanced the intranasal dosage forms to acquire certain medicinal goals.

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