IJMPR 2022, 6(7), 18-22

International Journal of Modern Pharmaceutical Research
www.ijmpronline.com

ISSN: 2319-5878
IJMPR
Review Article
SJIF Impact Factor: 5.273

HERBAL NASAL FORMULATION: A CRITICAL REVIEW

***[1]Harshit Yadav, [2]Vikas Srivastav and [3]Amresh Gupta**

[1]Research Scholar, Goel Institute of Pharmacy and Sciences, Lucknow (UP) IN.
[2,3]Faculty, Goel Institute of Pharmacy and Sciences, Lucknow (UP) IN.

Received on: 26/05/2022
Revised on: 16/06/2022
Accepted on: 06/07/2022

***Corresponding Author**
Harshit Yadav
Research Scholar, Goel Institute of Pharmacy and Sciences, Lucknow (UP) IN.

ABSTRACT

In the Ayurvedic system of Indian medicine, intranasal therapy has long been considered as a viable treatment option. Nasal medication administration is a good option for treatments that are effective at low doses but have low oral bioavailability. This review was focused on the polymers used, characterizations, advantages and limitations with herbs used in nasal formulations. Data was collected published in PubMed, Web of Science and various reputed platforms. The nasal route avoids the hepatic first-pass elimination that occurs with oral distribution, and it is simple to use and self-administer. Nasal drug delivery systems include nasal drops, nasal sprays, nasal gels and nasal powder. Various characterization parameters were used to evaluate such as pH, viscosity, isotonicity, drug content etc. Nasal formulations have numerous advantages i.e., fast delivery, self-administration, better patient compliance with some various limitations too. In conclusion, nasal spray medicine products are non-pressurized dispensers that provide a spray containing a metered dose of active component that is dissolved or suspended in solutions or mixes of excipients. Spray pattern, droplet size distribution, and Spray Content Uniformity are all critical characterization tests for nasal sprays that are affected by formulation and device parameters.

KEYWORDS: Herbal Nasal formulations, tulsi, drug content, characterization, isotonicity.

INTRODUCTION

In the Ayurvedic system of Indian medicine, intranasal therapy has long been considered as a viable treatment option. Many medications have been demonstrated to have improved systemic bioavailability when administered via nasal route rather than oral administration in recent years. Biotechnology has made a huge number of protein and peptide drugs available for the treatment of a wide range of ailments. These medications are not suited for oral delivery because they are rapidly destroyed in the gastrointestinal system or rapidly metabolised in the liver due to the first-pass action. For long-term therapy, even the parenteral route is inconvenient. So, after a number of different routes have been investigated, intranasal medication delivery has been proven to be quite promising for the administration of these drugs.[1] A number of good evaluations have been written in recent years.

Nasal drug delivery

Nasal medication administration is a good option for treatments that are effective at low doses but have low oral bioavailability. The nasal route avoids the hepatic first-pass elimination that occurs with oral distribution, and it is simple to use and self-administer. There are two types of nasally administered medicines on the market right now. The first group includes decongestants, topical steroids, antibiotics, and other over-the-counter (OTC) medications for the treatment of the nasal mucosa and sinuses, as well as low molecular weight and hydrophobic pharmaceuticals for the treatment of the nasal mucosa and sinuses. The second group of medications includes a handful that have significant nasal absorption to cause systemic effects. Due to their instability in the gastrointestinal tract, low absorption qualities, and rapid and efficient delivery, chemicals commonly provided by injection and rarely absorbed after oral administration are important possibilities.[2]

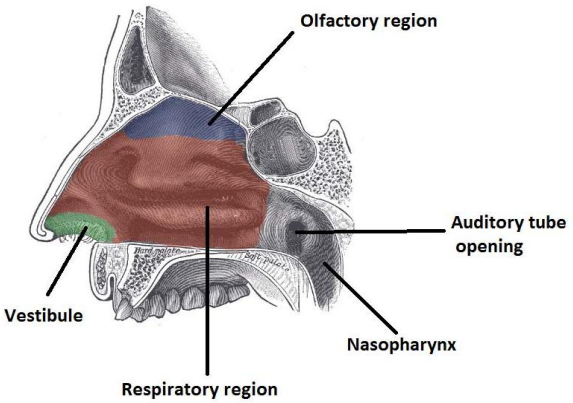

Fig. 1: Anatomy of nose.

The nasal septum, a central partition of bone and cartilage, divides the nasal cavity into two symmetrical halves; each half opens at the face via the nostrils and joins with the mouth at the naso-pharynx. The three primary regions of the nasal cavity are the nasal vestibule, respiratory region, and olfactory region. A folded structure on the lateral walls of the nasal cavity increases the surface area of the nose to roughly 150cm2. There are three turbinates in this folded structure: superior, medium, and inferior. The passageways of the main nasal airway are narrow, usually only 1-3mm wide, and this tight construction allows the nose to perform its primary duties.[3]

These are two segments that are connected in nasal system as below-

1. Olfactory region

The olfactory region of the human nose is located on the roof of the nasal cavities, immediately below the cribriform plate of the ethmoid bone that separates the nasal cavities from the cranial cavity. In contrast to the surrounding pink tissue, the olfactory tissue is frequently yellow. Humans have relatively basic nostrils because breathing is their major function, but other mammals have more complicated noses that are better equipped for olfaction.[5]

2. Respiratory region

This area is thought to be the primary site for medication absorption into the bloodstream. Ciliated columnar cells, non-ciliated columnar cells, goblet cells, and basal cells are the four main types of cells found in the respiratory epithelium. Neurosecretory cells are infrequent but can be spotted, although unlike basal cells, they do not extend into the airway lumen. Varied parts of the nasal cavity have different proportions of different cell types. Ciliated epithelial cells make up roughly 15-20% of the total number of cells in the lower turbinates, whereas non-ciliated epithelial cells make up 60-70%. As you get closer to the nasopharynx, the number of ciliated cells increases, while the number of non-ciliated cells decreases. The ciliated cells' job is to carry mucus from the mouth to the pharynx. The airway lumen is never reached by basal cells, which vary widely in quantity and shape. These cells have a low level of differentiation and serve as stem cells for other epithelial cells. Goblet cells, which include numerous secretory granules packed with mucin, make up around 5-15 percent of the mucosal cells in the turbinates. The goblet cells, in collaboration with the nasal glands, create secretions that form the mucus layer.[4]

Table 1: List of absorption enhancers used in nasal formulations.

Category	Compound
Surfactants	Polyozyethylene-9-lauryl ether (Laureth-9): Saponin
Bile salts	Trihydroxy salts (glycol- and taurocholate), Fusidic acid derivatives
Chelators	Salicylates Ethylenediaminetetraacetic acid (EDTA)
Fatty acid salts	Oleic acid, Caprylate Caprate, Laurate
Phospholipds	Lysophosphatidylcholine, Didecanoyl
Glycyrrhetinic acid Derivates	Carbenozolone, Glycyrrhizinate
Cyclodextrins	α, β, and γ- cyclodextrins and their derivatives
Glycols	n- glycofurols, n- ethylene glycols

Nasal drug delivery devices

Following devices.[6] are frequently employed in the delivery of nasal formulations-

Nasal drops

Nasal drops are one of the most straightforward and practical nasal administration techniques ever devised. The main downside of this technique is that it lacks dose precision, hence nasal drops may not be appropriate for prescription medications. Nasal drops are said to deposit human serum albumin more effectively in the nostrils than nasal sprays.

Nasal sprays

Nasal sprays can be made from both solution and suspension compositions. A nasal spray may deliver a precise amount from 25 to 200 m due to the availability of metered dose pumps and actuators. The size and shape (for suspensions) of the drug particles, as well as the viscosity of the formulation, influence the pump and actuator assembly that is used.

Nasal gels

Nasal gels are thickened liquids or suspensions with a high viscosity. There was little interest in this system until the recent introduction of a precise dosage device. The benefits of a nasal gel include reduced post-nasal drip due to high viscosity, reduced flavour impact due to reduced swallowing, reduced anterior leaking of the formulation, reduced discomfort due to soothing/emollient excipients, and targeting to mucosa for better absorption.

Nasal powder

If solution and suspension dosage forms are not possible to manufacture, such as due to medication stability issues, this dosage form may be developed. The lack of a preservative and the formulation's greater stability are two advantages of the nasal powder dose form.

Table 2: Drugs and delivery devices.

Drug	Delivery Device
Adrenal corticosteroids Jelly	Nasal spray, nasal drops, nasal insufflators, submucosal injections into the anterior tip of inferior turbine, metered dose aerosol
Antihistaminics	Nasal spray, nasal drops
Buserelin Formulations	Nasal spray, ointment
Calcitonin	Nose drops
Cocaine	Nasal spray, nose drops, cotton pledget, gauge packtail, insufflators, rubbing with cocaine mud
Dopamine	Nasal spray
Estradiol- 17β	Nasal spray, nasal drops, microsyringe
Gentaminin	Nasal spray
Hyoscine(scopolamine	Nasal spray, nasal drops
Insulin	Metered pump sprayer, metered dose aerosolized spray, fixed volume aerosol spray, nasal spray, nasal drops, cotton pledget
Isosorbidedinitrate	Nasal spray(isomack spray
Naferelin acetate	Nasal spray, tobacco snuff, injected into dogs frontal sinus
Nitroglycerin	Metered dose spray Instilled through Teflon i.v. Catheter
Oxytocin	Nasal spray, nasal drops, cotton pleadget, aerosol activated spray, graded polyethylene tube, direct instillation by tuberculin syringe and 25G needle
Progesterone	Nasal spray by an atomizer connected to a respiratory pump, nasal spray by gas atomizer, nasal solution administered by micropipette
Vaccines	Inhalation aerosol, nasal spray, nasal aerosol spray, nebulizer aerosol, nasal drops
Vitamin B12	Nose drops, insufflators
Xylometazoline	Nasal spray, nose drops

Characterization parameters

These factors are determined for nasal formulation mentioned as below-

Isotonicity

In the nasal medication delivery system, isotonicity is a crucial feature that should be appropriately managed.

pH

The pH of the nasal preparation should be the same as the pH of the nasal cavity to avoid irritation. It could be between 5.5 and 6.5. A pH metre is used to determine the pH. The pH of a nasal formulation is critical for several reasons.[7]

Viscosity

In gel formulations, viscosity is crucial. Gels offer lengthens the residence period, which is affected by viscosity. A viscometer is used to determine the viscosity of nasal gel. The viscosity was determined at a certain rpm for a specific period of time.

Gelation temperature

Various techniques, such as modified millers and the Donovan technique, can be used to determine the gelation temperature. In which 3 ml gel was transferred to test tubes and placed in a water bath with a 10°C temperature increase. The samples are checked for gelation, which is stated to occur when the meniscus no longer moves when tilted through 90ºC.

Drug content

In order to calculate the drug content, 1 ml of the formulation was placed in a 100 ml volumetric flask and the volume was increased to 100 ml using appropriate solvent. The amount of medicine on hand should be kept to a minimum.

Impurities

A validated analytical process or procedures should be used to determine the levels of contaminants and degradation products. Individual and total contaminants, as well as degradation products, should have acceptance criteria. According to the ICH rule for impurities, any relevant contaminants appearing at levels of 0.1 percent or higher should be stated.

Particle size

The droplet size is mostly affected by the device's design and management, such as the actuation parameters, as well as the formulation, with the most common median droplet size being between 30-120m. Deposition occurs mostly in the anterior regions of the nose if the droplets are too large (>120 m), and if the droplets are too small (>10 m), they can be inhaled and reach the lungs, which should be avoided for safety reasons. The specifications for both suspension and solution nasal sprays should include an acceptable control for the droplet size distribution of the delivered plume following spraying under defined experimental and instrumental settings.

Gel strength

Gel strength is determined by the following procedure: Taking 100gm of formulation in a 100ml graduated cylinder and neutralising it with NaOH can be used to determine the gel strength (0.5). The gel was then given a 70gm weight. The time (seconds) taken by the weight to penetrate 5 cm into the gel determines the gel strength, which is an indication of the nasalgel's viscosity at physiological conditions.[8]

Table 3: Plants and their parts used in nasal formulations.[9]

Plant	Scientific name	Part used
Kantakari	Solanum Xan-thocarpum	Whole plant
Brihati	SolanumIndicum	Root, Fruit
Pushkarmula	Inula Race-mosa	Root
Shati	Hedychium	Rhizome
Haritaki	Terminalia Chebula	Fruit
Pippali	Piper Longum	Fruit
Tulsi	Ocimum Sanc-tum	Leaves, Root, Seeds
Amalaki	Emblica Of0ici-nalis	Fruit

Advantages[10]

- Self-medication is made easier by easy access and needle-free drug application, which eliminates the requirement for trained people and improves patient compliance when compared to parenteral routes.
- Medicines with a low molecular weight, especially lipophilic drugs, penetrate the nasal mucosa well. Fentanyl, for example, has an absolute nasal bioavailability of roughly 80%.
- Due to the relatively wide absorption surface and strong vascularization, the drug absorbs quickly and has a quick onset of effect. In comparison to intravenous administration, the *Tmax* of fentanyl after nasal administration was less than or equivalent to 7 minutes. As an alternative to parenteral administration, nasal delivery of a relevant medicine would be effective in emergency therapy.
- Preventing the gastrointestinal tract from being exposed to extreme environmental conditions (chemical and enzymatic degradation of drugs).
- Avoidance of hepatic first-pass metabolism, allowing for a lower dose when compared to oral administration.
- Possibility of direct medication delivery to the central nervous system via the olfactory system, bypassing the blood-brain barrier.
- Induction of a secretory immune response at a distant mucosal site via direct vaccine administration to lymphatic tissue.

Limitations[11]

- The histopathological toxicity of absorption enhancers employed in nasal medication delivery systems is still unknown.
- Patients find it inconvenient when compared to oral delivery systems since nasal discomfort is a potential.
- When compared to the GIT, the nasal cavity has a lesser absorption surface area.
- Both the substance and the ingredients added to the dosage form pose a risk of local side effects and irreversible damage to the cilia on the nasal mucosa.
- The common cold, as well as other pathological disorders involving mucociliary dysfunction, can have a significant impact on the rate of nasal clearance and, as a result, the therapeutic efficacy of nasally given drugs.
- The dosage form could be mechanically lost and end up in other sections of the body.

CONCLUSION

Nasal medication delivery has progressed to a new level in the scientific community. Nasal medication administration is a viable alternative to injection drug delivery. More medications intended for systemic absorption in the form of nasal formulation are likely to hit the market in the near future. On the long run, several formulation elements will impact the development of a drug with a drug delivery system; new nasal products for the treatment of long-term disorders such diabetes, growth deficit, osteoporosis, fertility treatment, and endometriosis are also expected to be sold. Pharmaceutical corporations, on the other hand, are pouring money into the development of nasal medication products in response to the increased demand for them in the worldwide pharmaceutical market.[12]

Nasal spray medicine products are non-pressurized dispensers that provide a spray containing a metered dose of active component that is dissolved or suspended in solutions or mixes of excipients. Spray pattern, droplet size distribution, and Spray Content Uniformity are all critical characterization tests for nasal sprays that are affected by formulation and device parameters.

Funding

Nil.

Conflict of Interest

None.

REFERENCES

1. Chein Y W, Su KSE and Chang SF. Nasal systemic drug delivery. Dekker, 1989; 1-77.
2. Wearle LL. Crit.Rev.her.Drug carrier. Sst, 1991; 8: 331-394
3. J Pharm PharmaceutSci (www.cspsCanada.org), 2009; 12(3): 288 – 311.
4. Chipper, et al. The nasal mucociliary clearance: relevance to nasal drug delivery. Pharma Res., 1991; 7: 807-814.
5. Junginger. Bioadhesive polymer system for peptide delivery. Acta Pharma Tech, 1990; 36: 110-12.
6. Chanler SG, Illum, L and Thomas,NW. int J Pharm, 1991; 76: 61-70
7. Nandgude. T., Thube. R., Jaiswal. N., Deshmukh. P., Chatap. P.V, Hire. N. Formulation and Evolution of pH Induced in situ nasal gel of Salbutamol Sulphate, Internationaljournal pharmaceutical Science nanotechnology 2008; 1: 177-182.
8. Witschi C, Mrsny RJ. In vitro evaluation ofmicroparticles andpolymer gels for use asnasalplatforms for protein delivery. Pharm Res, 1999; 16: 382–390.
9. Ashiya A S Azim1, Dhirajsingh Rajput. Drugs For Ayurvedic Hand Sanitizer and Nasal Spray And Its Method Of Preparation. Int. J. Res. Pharm. Sci., 2020; 11(1): 310-316.
10. Kao HD, et al. Enhancement of the systemic and CNS specific delivery of L-dopa by the nasal administration of its water-soluble prodrugs. Pharm Res., 2000; 17: 978-984.
11. Hirai S, et al. Absorption of drugs from the nasal mucosa of rats. Int J Pharm, 1981; 7: 317-325.
12. Nirav S Sheth, Rajan B Mistry. A Review: Nasal Drug Delivery System. Research J. Pharm. and Tech, 4(3): 349-355.