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NASAL SPRAY FOR DECONGESTANT THERAPY

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Abstract:

Nasal spray formulations have emerged as a reliable, non-invasive, and rapid-acting alternative for decongestant therapy. The common cold has no known cure, and the only way to treat nasal congestion is with symptomatic medications. The nasal route offers both local and systemic drug delivery advantages, including avoidance of first-pass metabolism, rapid onset of action, and high patient compliance. Nasal sprays are preferred over drops or powders due to better dose precision and patient acceptability. However, limitations include limited absorption for large or polar drugs, mucosal irritation risks, enzymatic degradation, and volume constraints. Continuous improvements in formulation technology, such as preservative-free systems and mucoadhesive agents, promise enhanced safety and therapeutic performance in future nasal drug products.

Keywords: *Nasal cavity, Anatomy, Absorption,mechanism,challenges,Adv,Dis, Application .*

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INTRODUCTION:

It is acknowledged that intranasal drug administration is a practical and dependable substitute for parenteral and oral methods. Both local and systemic medication administration are possible with the nasal route. For example, nasal cavity disorders such congestion, rhinitis, sinusitis, and associated allergy diseases are typically treated with localized nasal medication delivery.

More focus has recently been placed on exploiting the nose as the body's entrance point to achieve a systemic medication activity. Additionally, nasal distribution appears to be a good method of getting across the (BBB) blood-brain barrier, enabling direct drug delivery in the biophase of substances that are active in the central nervous system.The nasal spray dosage form has a good patient compliance rate since it is affordable, portable, and self-administrable. As a result, nasal drug delivery has gained popularity as a drug administration method and has significant room for expansion.

Acute rhinosinusitis caused by bacteria or viruses can also result in nasal congestion. Allergy prevalence has increased worldwide, with rates of AR ranging from 1 to 18% This has contributed to the emergence of the so-called "allergy epidemic" of the twenty-first century and may be caused by genetic, lifestyle, and environmental factors.

The common cold has no known cure, and the only way to treat nasal congestion is with symptomatic medications.

Nasal Anatomy

- **Gross compartments**: Each side of the nose forms a nasal cavity separated by the nasal septum; posteriorly both open into the choanae → nasopharynx.
- **Regions**:
  - **Vestibule** — just inside nostrils; lined by skin with coarse hairs (vibrissae).
  - **Respiratory region** — largest area, lined by pseudostratified ciliated columnar epithelium with goblet cells and glands. Responsible for mucus secretion and MCC.
  - **Olfactory region** — superior part (olfactory cleft) containing olfactory receptor neurons, sustentacular/supporting cells and basal (stem) cells.
- **Bony framework & turbinates**: Lateral walls bear superior, middle and inferior conchae (turbinates) — increase surface area and create turbulent flow to improve conditioning and particle deposition.
- **Blood supply & innervation**: Rich vascular supply (sphenopalatine, anterior ethmoidal, superior labial branches) → important for humidification and for common epistaxis sites. Sensory innervation: trigeminal; olfactory nerve (CN I) for smell.[5]

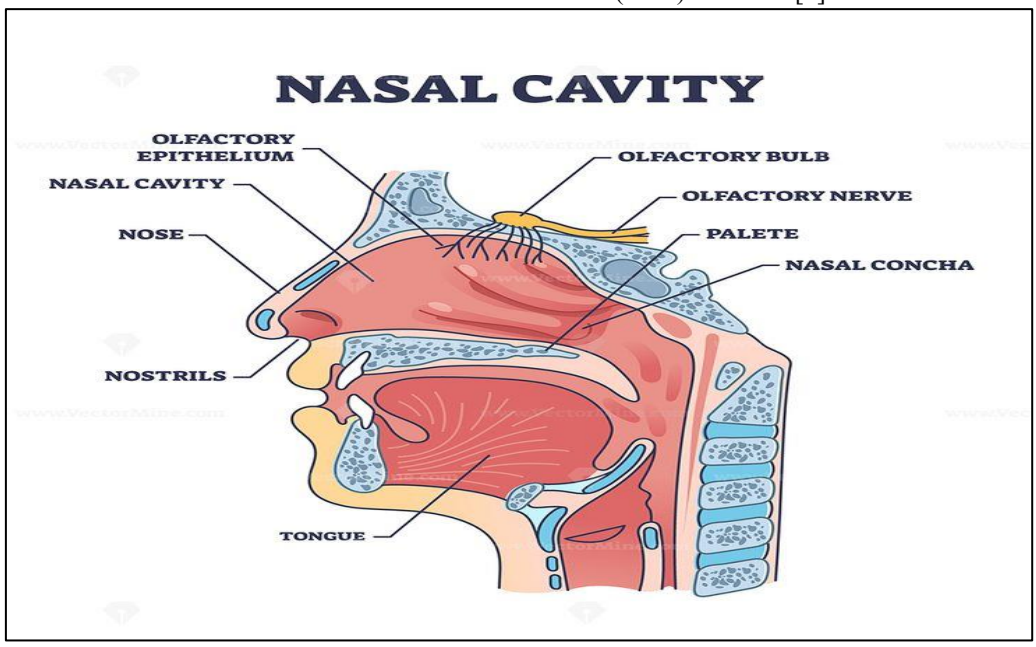

Fig.1 Anatomy of nose

- **Physiology :-**

- **Air conditioning**: Large mucosal surface, rich vasculature and turbulent flow across turbinates warm and humidify air — preserving airway mucosa and optimizing gas exchange.
- **Filtration & mucociliary clearance (MCC)**: Mucus traps particles and cilia transport mucus toward the nasopharynx (or anteriorly) — first line mechanical defense. MCC rate varies by region and can be altered by drugs, disease, age.
- **Olfaction**: Odorants transported to the olfactory epithelium (olfactory cleft); olfactory receptor neurons transduce chemical signals to the olfactory bulb.
- **Nasal cycle & vascular dynamics**: Alternating partial congestion of turbinates (nasal cycle) changes resistance and airflow distribution; autonomic control of mucosal blood flow modulates this.
- **Immunologic roles**: The mucosa is immunologically active (mucus, antimicrobial peptides, immunoglobulins, resident immune cells) — key for innate defense and shaping adaptive responses to inhaled antigens.

Formulation of Nasal Spray:-

Components — what to include and why

1. **Active**
   - Oxymetazoline HCl 0.05% w/v (0.5 mg/mL) — common OTC strength.
   - Xylometazoline HCl 0.05% w/v (or up to 0.1% for some products).[9]
2. **Buffer system (pH control)**
   - Common buffers: **phosphate (NaH2PO4/Na2HPO4)** or **citrate** systems. Patents and formulations often use phosphate to target pH 3–6.
3. **Tonicity agent**
   - **Sodium chloride** to ~0.9% for isotonic solution; some formulations use 0.5% NaCl for mild hypotonicity (improves uptake for some actives) — test comfort and mucociliary clearance.
4. **Preservative** *(if multi-dose non-sterile presentation)*
   - **Benzalkonium chloride (BKC)** (typical 0.01% w/v) — effective, widely used, but has literature reporting mucosal effects with chronic use; weigh pros/cons. Alternatives: **potassium sorbate**, **phenoxyethanol**, or preservative-free unit dose pumps.
5. **Viscosity / mucoadhesive agents** (optional — to increase residence time)
   - **Low-level HPMC (hypromellose)** or **Carbopol** (very low %), **HA (hyaluronic acid)**, **iota-carrageenan**, **CMC** or **Poloxamer** for in-situ gelling. These increase contact time and may reduce dosing frequency;
6. **Humectants and cosolvents**
   - **Glycerin (2–5% w/v)**, **PEG 400 (small %)** — improve spray feel and reduce stinging for some APIs. Keep cosolvents low to avoid altering spray device performance.
7. **Antioxidants / chelators** (if needed)
   - **EDTA** (chelating agent) can stabilize trace-metal sensitive APIs and may boost preservative efficacy at low levels (e.g., 0.01–0.05%). Test for compatibility.
8. **Water for injection** (WFI) — for sterile or aseptic processing when required.

❖ **Mechanism of action :-**

. Oxymetazoline hydrochloride (nasal decongestant spray)

- Oxymetazoline is a topical α-adrenergic receptor agonist (primarily α_1, possibly α_2) on the smooth muscle of blood vessels in the nasal mucosa
- . **Types of Nasal Drugs Delivery Spray:-**

1. Nasal drops and sprays

The most straightforward and practical method created for nasal administration is nasal drops. According to reports, nasal drops are more effective than nasal sprays at depositing human serum albumin in the nostrils.

2. Nasal gels

Nasal gels are thickened liquids or suspensions with a high viscosity. A nasal gel's benefits include reducing postnasal drip from its high viscosity, reducing taste impact from swallowing less.

Advantages of Nasal Drug Delivery System

- Drugs absorbed orally can be delivered to systemic circulation by means of nasal drugs delivery.
- Hepatic first pass metabolism is avoided.
- Easy accessibility.
- Self- medication is possible.

Disadvantages of Nasal Drug Delivery System

- Nasal cavity provides smaller absorption surface area when compared to GIT.
- Relatively inconvenient to patient who compared oral delivery system since there is possibility of irritation.
- There is a risk of local side effects and irreversible damage of the cilia on

the nasal mucosa, both from the substance and from constituents added to the dosage form.

Mechanism of drug absorption through nose

Drugs absorbed from the nasal cavity pass through the mucus layer it is the initial step towards absorption. This layer allows small layer, uncharged medications to flow easily, but larger, charged substances struggle to do so. Drug absorption through the nose occurs via two processes.

- **Paracellular transport**

Transferring chemicals across the epithelium involves going via intercellular gaps between cells. This aquatic transport method is slow and passive.[19]

- **Transcellular transport**

It is described as the movement of solutes within a cell. Transport via a lipoidal membrane is involved. It is a carrier-mediated active transport method.[20]

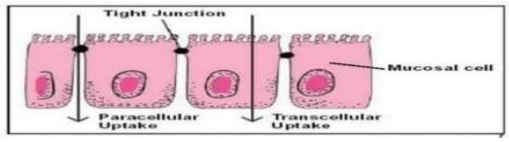

Fig.2 Mechanism of absorption

Barriers of Nasal absorption

- **Low bioavailability**

Lipophilic drugs are generally well absorbed from the nasal cavity compared to polar drugs. It is due to low membrane permeability.

- **Low membrane transport**

Rapid clearance of the administered formulation from the nasal cavity due to the mucociliary clearance mechanism.

Enzymatic Degradation

Low transport of especially peptides and proteins across the nasal membrane is the possibility of an enzymatic degradation of the molecule either within the lumen of the nasal cavity or during passage across the epithelial barrier by exopeptidase and endopeptidase.

Formulation of nasal spray

Nasal spray drug products contain therapeutically active ingredients (drug substances) dissolved or suspended in solutions or mixtures of excipients (e.g., preservatives, viscosity modifiers, emulsifiers, buffering agents) in no pressurized dispensers that deliver a spray containing a metered dose of the active ingredient.

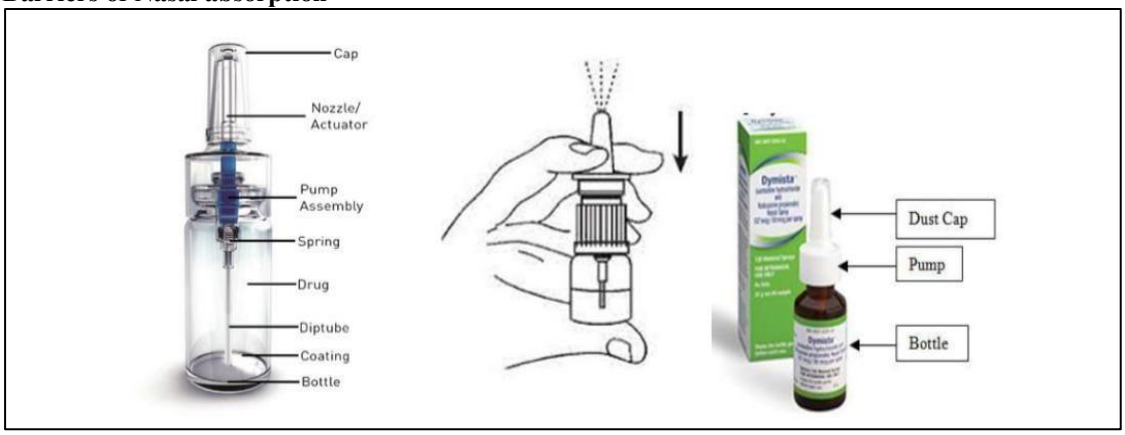

Fig.3 Nasal Sprays

Table 1: Commonly utilized Excipients

Category	Role	Example	IIG limits for nasal sprays (%w/w)
Tonicity Adjusting agent	Used as adjust tonicity of formulation	NaCl, Anhydrous Dextrose	0.9 0.5
pH Adjustment	Use to adjust pH same to physiological conditions and maximize drugs stability	Sodium hydroxide, Sulphuric acid, Hydrochloride acid	0.004 0.4
Purging	Used to reduce oxidation	Butylated hydroxyl toluene Butylated hydroxyl anisole	0.01 0.0002
Antimicrobial preservative	To avoid microbial growth in the	Benzyl alcohol Benzalkonium chloride	0.0366

	formulation	Chlorobutanol Propylene glycol	0.119 0.5 20
Buffer component	It gives buffer capacity to formulation at desired pH	Anhydrous trisodium citrate	0.0006
Surfactant	Increases viscosity and suspendability of suspension	CMC-Na	0.15
Cation chelating agent	Forms chelate with ions present in formulation and increases stability	Disodium EDTA	0.5
Suspending agent	Increase viscosity and suspendability of suspension	CMC-Na	0.15
Co-solvent	Helps to improve solubility	Alcohol PEG 400 Propylene glycol	2 20 20
Humectant	Used to maintain humidification in formulation	Glycerin	0.233

Challenges of Nasal Drug Delivery

- Nasal geometry and site of drug deposition

Nasal drug delivery system is more effective for local action, systemic action, and central nervous system action, at lower doses with minimum side effects. However, delivering drug to the specific regions is challenging.

Mucociliary clearance

It plays an important role in therapeutic activity of drug in posterior nasal cavity so that absorption occurs more quickly.

Other challenges are as follows:

- Drug diffusion through mucus layer and transport across respiratory epithelial membrane.
- Potential degradation by extracellular and intracellular enzyme systems.

Majority of nasal formulations are prepared by use of active pharmaceutical ingredient (API) and various excipients like preservatives, suspending agents, emulsifiers, buffering agents etc.

Characterization of Nasal Sprays

- pH

Osmolality

Viscosity

Spray Content Uniformity (SCU)

Applications

❖ Delivery of non-peptide pharmaceuticals

Delivery of peptide-based pharmaceuticals

Delivery of Drugs to Brain through Nasal Cavity

Delivery of Vaccines through Nasal Route

❖ **Quality Control (QC) Tests**

1. Organoleptic Evaluation

Purpose:

To assess the *appearance, odor, and clarity* of the nasal spray formulation to ensure uniformity and acceptability.

Procedure:

- Visually inspect the solution under white light for color, clarity, and absence of particulate matter.
- Evaluate odour using a trained panel (2–3 analysts).
- Note any phase separation or precipitation.

Typical Acceptance Criteria:

- Clear, colourless or slightly coloured liquid.
- Odour should be characteristic and acceptable (no foul smell).
- No turbidity or particulate matter visible.

2. pH Determination

Purpose:

To ensure compatibility with nasal mucosa and stability of the drug substance.

Procedure:

- Use a **calibrated digital pH meter**.
- Measure the pH of the formulation at room temperature (25 °C).
- Perform in triplicate and calculate mean ± SD.

Typical Acceptance Criteria:

- pH between **4.5 and 6.5** (compatible with nasal mucosa).
- No significant deviation during stability testing.

Example Reading:

Batch	pH (Mean ± SD)
A	4.62 ± 0.02
B	4.59 ± 0.01
C	4.70 ± 0.02

3. Spray Pattern

Purpose:

To confirm that the spray forms a uniform and symmetrical pattern ensuring dose reproducibility.

Procedure:

- Hold the nasal spray 30 mm away from a paper sheet.
- Actuate 3–5 times.

Example Reading:

Actuation	Diameter (mm)	Circularity
1	22.5	0.95
2	23.0	0.96
3	22.8	0.95

- Measure the diameter and shape using image analysis or laser light projection.
- Calculate circularity or aspect ratio.

Typical Acceptance Criteria**:**

- Circular spray pattern (no streaking or tails).
- Diameter between 20–25 mm at 30 mm distance.
- Circularity index > 0.9.[35,36]

4. Droplet Size Distribution

Purpose:

Determines particle size to predict drug deposition in the nasal cavity.

Procedure:

- Use Laser Diffraction Analyzer (e.g., Malvern Spraytec).
- Measure Dv10, Dv50, Dv90 (droplet size percentiles).
- Calculate SPAN = (Dv90 - Dv10) / Dv50 to assess uniformity.

Typical Acceptance Criteria:

- Dv50 (median droplet size): 40–60 µm
- SPAN**:** < 2.0 (indicates narrow size distribution)[33]

Example Reading:

Actuation	Dv10 (µm)	Dv50 (µm)	Dv90 (µm)	SPAN
1	24.8	54.6	110.3	1.57
2	25.1	55.2	111.0	1.56
3	24.9	55.0	110.7	1.56

5. Sterility / Microbial Limit Testing

Purpose:

Ensures that nasal spray is free from harmful microorganisms, especially for aqueous formulations.

Procedure:

- Perform Sterility Test (USP <71> or IP 2021) by membrane filtration or direct inoculation.
- Incubate in Fluid Thioglycollate Medium (FTM) and Soybean Casein Digest Medium (SCDM) for 14 days at 30–35 °C and 20–25 °C respectively.
- Observe for microbial growth.

For preserved multi-dose sprays, perform Preservative Efficacy (Challenge Test) against:

Typical Acceptance Criteria (per USP <51>):

- ≥ 3 log reduction by 14 days for bacteria,
- ≥ 1 log reduction for fungi by 14 days.[32]

Example Reading (log10 CFU/mL):

Organism	Day 0	Day 7	Day 14	Day 28	Log Reduction (28)
S. aureus	6.0	2.1	1.5	1.2	4.8
P.aeruginosa	6.0	2.5	2.0	1.8	4.2
C.albicans	6.0	4.8	4.5	4.2	1.8

Available Nasal Spray Products in the Market

Otrivin is one of the most commonly used nasal decongestant sprays. It contains *Oxymetazoline Hydrochloride* at a concentration of 0.05% w/v in an aqueous buffered vehicle, often preserved with *Benzalkonium Chloride (0.01% w/v)*.

Fig.4 Otrivin oxy nasal spray

Nasivion is another widely marketed nasal spray containing *Oxymetazoline Hydrochloride 0.05% w/v* as the active ingredient. It provides quick and effective relief from nasal congestion caused by colds, sinusitis, and allergic rhinitis.

Fig.5 Nasivion Nasal drop

Vicks Sinex nasal spray also contains *Oxymetazoline Hydrochloride 0.05% w/v* as the active component. It is indicated for the temporary relief of nasal congestion due to the common cold, sinusitis, or allergies. The product is available in medicated and saline variants, such as *Sinex Severe* and *Sinex Ultra-Fine Mist*.

Fig.6 Vics Sinex nasal spray

Summery

The review discusses nasal sprays as an effective drug delivery system, primarily for treating nasal congestion and related respiratory conditions. The nasal route offers both local and systemic drug delivery advantages, including avoidance of first-pass metabolism, rapid onset of action, and high patient compliance. The anatomy and physiology of the nasal cavity—especially its vascularity, surface area, and mucociliary clearance—make it a favorable site for drug absorption. Formulation components of nasal sprays typically include active agents such as Oxymetazoline Hydrochloride or Xylometazoline Hydrochloride, buffers for pH control, tonicity agents like sodium chloride, preservatives, viscosity enhancers, humectants, and antioxidants. Each excipient plays a role in optimizing stability, comfort, and therapeutic efficiency. Mechanistically, oxymetazoline acts as an α-adrenergic agonist, producing vasoconstriction in nasal mucosa to relieve congestion. Nasal sprays are preferred over drops or powders due to better dose precision and patient acceptability. However, limitations include limited absorption for large or polar drugs, mucosal irritation risks, enzymatic degradation, and volume constraints.

CONCLUSION:

Nasal spray formulations have emerged as a reliable, non-invasive, and rapid-acting alternative for decongestant therapy. Their design allows targeted delivery to the nasal mucosa, resulting in efficient drug absorption and immediate symptomatic relief. Despite their benefits, proper usage and adherence to recommended duration (generally not exceeding five to seven days) are crucial to prevent adverse effects such as rebound congestion and mucosal irritation.

Overall, nasal sprays represent a valuable advancement in pharmaceutical drug delivery, combining convenience, efficacy, and patient compliance. Continuous improvements in formulation technology, such as preservative-free systems and mucoadhesive agents, promise enhanced safety and therapeutic performance in future nasal drug products.

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