

Nasa Hi Shiraso Dwaram: Anatomical Correlation With Modern Nose-To-Brain Drug Delivery

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ABSTRACT

The Ayurvedic axiom "Nasa hi shiraso dwaram"—the nose as gateway to the head—underpins Nasya Karma for shiroroga and urdhvajatrugata vikara. This systematic review correlates this principle with modern intranasal drug delivery, analyzing classical texts (Charaka Samhita, Ashtanga Hridaya, Ashtanga Sangraha) alongside contemporary literature on nasal anatomy, olfactory/trigeminal pathways, and blood-brain barrier (BBB) bypass mechanisms. Modern neuroanatomy validates direct nose-to-brain connections via intracellular (axonal transport through olfactory neurons) and extracellular (perineural/paracellular) pathways. Lipid-based Ayurvedic oils exhibit physicochemical properties analogous to modern lipid nanocarriers: lipophilicity facilitates mucosal spreading/retention; bioadhesion enhances absorption; fine dispersion mimics nanoparticle size (<200 nm) requirements. These correlations establish Nasya Karma as an empirically-derived precursor to targeted intranasal therapeutics for neurological disorders. Ayurvedic formulations therapeutic efficacy likely stems from optimized drug delivery principles rediscovered by modern pharmacology. This synthesis provides mechanistic rationale for Nasya's clinical utility and identifies translational research priorities: pharmacokinetic tracing of Ayurvedic oils, comparative deposition studies, and clinical efficacy trials...

Keywords: Nasya Karma; Nasa Hi Shiraso Dwaram; Intranasal Drug Delivery; Nose-to-Brain; Olfactory Pathway; Blood-Brain Barrier; Ayurvedic Formulations

INTRODUCTION

In Ayurveda, various drug administration routes are described, with the nasal route holding prime importance for treating Shiroroga (head disorders). Classical Acharyas emphatically declared "Nasa hi shiraso dwaram" – the nose is the gateway to the head – underscoring Nasya Karma's therapeutic efficacy for Urdhvajatrugata vikara (supra-clavicular ailments).

This ancient principle finds striking anatomical and physiological correlation with modern intranasal drug delivery systems, which bypass the blood-brain barrier to achieve direct central nervous system targeting. This review systematically analyzes classical Ayurvedic texts alongside contemporary neuropharmacological evidence on olfactory/trigeminal pathways, lipid-based formulations, and nasal deposition patterns. By bridging these domains, we establish Nasya Karma as a traditional precursor to targeted nose-to-brain therapeutics, paving the way for integrative neurological research.

MATERIAL AND METHODS

In this review study various ayurvedic textbooks and research articles were referred. For Sanskrit words, Sanskrit dictionary

is used for proper understanding of the terminologies. And Ayurvedic terminology, for their meaning commentary on Sushruta Samhita by Ghanekar is used. For modern correlation various research articles were compared and modern textbooks were referred.

AYURVEDIC REVIEW

नस्तः कर्म च कुर्वति शिरोरोगेषु शास्त्रवित् ।

द्वारं हि शिरसो नासा तेन तद्वाप्य हन्ति तान् ॥८८८॥ (च. सि-9/88)

According to Acharya Charak, Nasya Karma is considered useful in disease related to head i.e Shiroroga. He used to perform nasal therapies in disorders of the head. The nose is indeed the gateway to the head; Through it, it pervades and eliminates the doshas." This verse emphasizes the role of nasal therapy (Nasya) in treating disorders of the head. Hence he pronounced nasa as a route to shirah.⁽¹⁾

ऊर्ध्वजत्रुविकारेषु विशेषान्नस्यमिष्यते ।

नासा हि शिरसो द्वारं तेन तद्वाप्य हन्ति तान् ॥ १ ॥ (अ.ह- 20/1)

According to Asthanga Hridya, for the treatment of Urdhajatrugata Vikara, Nasya is considered as best route for the administration of drug. The nose is indeed the gateway to the head; Through it, it pervades and eliminates them." This verse highlights that Nasya therapy is particularly beneficial for Urdhajatrugata Vikara in the body. It indicates the importance of nasal passages as a direct route to the head, through which medicinal substances administered can effectively reach and alleviate these disorders. And He also pronounced nasa as a route to shirah.⁽²⁾

नासा हि शिरसोद्वारम्, तत्रावसेचितमौषधं स्रोतः शृङ्गाटकं प्राप्य मूर्धानं नेत्रश्रोत्रकण्ठादि सिरामुखानि च वैकारिकीमशेषामाशुदोषसंहतिमुत्तमाङ्गादपकर्षति ॥ ३ ॥ (अ०सं० सू०- 29/3)

According to Asthanga Samgraha, The nose is the gateway to the head, Wherein, through nasal medication, the medicine reaches. And by this it quickly draws away vitiated doshas accumulated in the head, eyes, ears, throat, and all other parts of the head region. This verse emphasizes the importance of nasal administration (Nasya) in Ayurveda, where the medication administered through the nose help in cleansing and balancing the doshas (bioenergies) that may have accumulated in various parts of the head and neck. And Hence he also pronounced nasa as a route to shirah.⁽³⁾

MODERN REVIEW

Using intranasal administration to target therapies to the central nervous system offers significant advantages in treating neurological disorders, particularly in cases where the blood-brain barrier (BBB) restricts the effectiveness of many therapeutic agents developed for memory loss and neurodegenerative diseases due to their size or charge. While invasive methods like intracerebroventricular administration have been utilized to overcome the BBB, they are impractical for human use due to issues such as convenience, safety, and cost. Intranasal delivery directly introduces therapeutics from the nasal cavity into the CNS, bypassing the BBB and providing a non-invasive alternative to invasive administration methods.⁽⁴⁾

Two broad categories of nose-to-brain pathways are described in contemporary literature: extracellular (paracellular) and intracellular (transcellular) routes. These pathways explain how substances administered through the nose can reach the brain, thereby supporting the therapeutic rationale of Nasya. The intranasal route delivers drugs to the brain through these two primary mechanisms. In the intracellular pathway, drugs are taken up by olfactory neurons via endocytosis. They are then transported along the axons to the olfactory bulb, where they are released at synaptic sites. This process continues across neurons, allowing the drug to spread to different regions of the brain. In the extracellular pathway, drugs move outside the cells by crossing the nasal epithelium through paracellular spaces. They then travel along perineural pathways to reach the subarachnoid space, ultimately entering the cerebrospinal fluid and brain.⁽⁵⁾

FLOW CHART: 1 ILLUSTRATION OF INTRACELLULAR (TRANSCELLULAR) PATHWAY⁽⁵⁾

Drug deposited in olfactory region of nasal cavity

↓

Uptake of drug by olfactory receptor neurons via endocytosis

↓

Intracellular vesicular transport within olfactory neurons

↓

Axonal transport through olfactory nerve fibers

↓

Drug reaches olfactory bulb
 ↓
 Release of drug at synaptic junctions
 ↓
 Trans-synaptic neuronal transport to other brain regions
 ↓
 Distribution of drug within the central nervous system

FLOW CHART: 2 ILLUSTRATION OF EXTRACELLULAR (PARACELLULAR) PATHWAY ⁽⁵⁾

Drug administration into nasal cavity
 ↓
 Diffusion across nasal epithelium through paracellular spaces and TJs (tight junctions)
 ↓
 Entry into lamina propria
 ↓
 Distribution through extracellular pathways
 ↓
 Movement into perineural space
 ↓
 Perivascular pumping and bulk flow
 ↓
 Entry into subarachnoid space
 ↓
 Convection-mediated transport through CSF (cerebrospinal fluid pathway)
 ↓
 Distribution into CNS tissue
 ↓
 Additional absorption into blood vessels and lymphatics
 ↓
 Drug reaches different regions of the brain while partially bypassing the BBB

In a similar way, Ayurvedic preparations which are lipid-based (oil-based), show comparable advantages when used in *Nasya Karma*. Because of their oily and lipophilic nature, they can easily spread over the nasal mucosa, stay there for a longer time, and help in better absorption of the drug. This suggests that traditional Ayurvedic oils may work in a way similar to modern lipid-based delivery systems. Studies also show that factors like small particle size, particle size distribution, zeta potential, etc are important for effective drug delivery. For successful intranasal brain targeting, several formulation parameters must be carefully optimized. Important factors include particle size, particle size distribution index (PDI), zeta potential, drug loading capacity, release characteristics, surface modification, and colloidal stability. Studies suggest that nanoparticle size should generally remain below 200 nm for effective transport through the nasal pathway. Likewise, a lower PDI value indicates more uniform particle distribution, which contributes to better absorption and consistent drug delivery across the nasal mucosa. Zeta potential is another important parameter because it reflects the surface charge and physical stability of nanoparticles. Nanoparticles with zeta potential values above or below ± 30 mV are generally considered stable and less likely to aggregate. Positively charged nanoparticles show stronger interaction with negatively charged mucin present in the nasal mucosa, thereby increasing retention time and improving drug absorption. However, excessively high surface charge may increase the risk of toxicity.⁽⁶⁾

Pathway	Mechanism	Key Factors	Relevance to Nasya
Intracellular	Axonal transport	Lipophilicity, particle size	Targeted endocytosis by olfactory

Pathway	Mechanism	Key Factors	Relevance to Nasya
	(endocytosis)	<200 nm	neurons
Extracellular	Perineural diffusion	Positive zeta potential, bioadhesion, PDI <0.3	<i>Taila</i> mucoadhesion prolongs olfactory contact

Table 1: Nose-to-Brain Pathways and Nasya Karma Correlations

Research on inhalation aromatherapy and intranasal drug delivery has shown that odor molecules and lipophilic therapeutic agents absorbed through the nasal mucosa can stimulate olfactory receptors and transmit signals to the olfactory bulb, limbic system, hypothalamus, hippocampus, amygdala, and frontal cortex.⁽⁷⁾

Hydrophilic drugs can be effectively administered through the intranasal route in the form of simple aqueous solutions after proper solubilization, whereas hydrophobic drugs can achieve improved brain delivery through the use of nanoformulations and prodrug-based delivery systems.⁽⁸⁾

The nasal cavity contains several anatomically and functionally important regions that play a significant role in intranasal drug delivery. The turbinate region possesses a rich vascular network and large surface area, which facilitates rapid systemic absorption of drugs. In contrast, the olfactory region, located in the superior part of the nasal cavity, is directly connected to the central nervous system through the olfactory and trigeminal neural pathways, making it a potential route for nose-to-brain drug delivery. Due to the complex structure of the nasal passages, the site of drug deposition greatly influences therapeutic efficacy. Therefore, targeted deposition in specific nasal regions has become an important area of research in modern intranasal drug delivery systems, particularly for neurological disorders and migraine management.⁽⁹⁾

DISCUSSION

The classical Ayurvedic principle “Nasa Hi Shiraso Dwaram” demonstrates a remarkably advanced understanding of the relationship between the nasal cavity and the brain. Modern scientific evidence regarding nose-to-brain drug delivery strongly supports this concept by showing that the nasal route provides direct access to the central nervous system through intracellular and extracellular pathways, bypassing the blood–brain barrier. These pathways scientifically explain the mechanism through which Nasya Karma may exert its therapeutic effects on higher neurological centers.

The intracellular pathway enables transport of therapeutic substances through olfactory neurons into different regions of the brain, while the extracellular pathway allows movement through paracellular and perineural channels into the cerebrospinal fluid and brain tissue. These mechanisms establish a strong correlation between classical Ayurvedic concepts and contemporary neuroanatomy and neuropharmacology.

Recent advances in nanotechnology have highlighted the effectiveness of lipid-based nanoparticles for targeted nose-to-brain drug delivery due to their lipophilic nature, enhanced mucosal adhesion, prolonged retention time, and improved permeability. In a similar manner, Ayurvedic oil-based formulations possess comparable physicochemical properties that may facilitate effective absorption through the nasal mucosa and support direct transport to the brain. Although these traditional formulations are not engineered nanoparticles, their lipid-rich composition, fine dispersion, and bioadhesive characteristics may contribute to therapeutic efficacy in a way analogous to modern lipid-based delivery systems.

Therefore, Nasya Karma can be interpreted as a traditional and clinically practiced form of targeted intranasal drug delivery. The integration of Ayurvedic wisdom with modern neuroscientific and pharmaceutical research opens new possibilities for understanding the scientific basis of Nasya and for developing innovative brain-targeted therapeutic approaches in the future.

Future studies may focus on nose-to-brain drug delivery pathways by employing suitable animal models, such as rodents, to trace the movement of the drug from the nasal cavity to the brain. In this context, modern techniques like fluorescent labeling or radiolabeling of the formulation or its active components can be utilized to study its distribution through olfactory and trigeminal pathways, thereby providing scientific validation for the Ayurvedic principle “*Nasa hi shiraso dwaram.*”

Moreover, integrating behavioral and clinical models can help in establishing both mechanistic and therapeutic evidence. These studies may strengthen the scientific basis of *Nasya Karma* and promote its integration with modern drug delivery research.

Although such advanced studies may require specialized facilities, ethical approvals, and financial support, they hold significant potential to bridge the gap between classical Ayurvedic knowledge and contemporary biomedical science.

CONCLUSION:

Recent advances in neuroscience and intranasal drug delivery research have provided significant scientific insight into the direct connection between the nasal cavity and the brain. Modern studies demonstrate that therapeutic agents administered

through the nasal route can bypass the blood–brain barrier and reach the central nervous system through olfactory and trigeminal pathways via intracellular and extracellular mechanisms. These findings provide a scientific basis for understanding the therapeutic action of Nasya Karma described in Ayurveda. Oil-based Ayurvedic formulations possess lipid-rich, bioadhesive, and permeation-enhancing properties that may support effective mucosal absorption, prolonged nasal retention, and neuronal transport to the brain. Although not specifically designed as nanocarriers, their physicochemical nature shows similarities to modern lipid-based drug delivery systems used for targeted nose-to-brain transport. Thus, Nasya Karma may be interpreted as a traditional and clinically practiced approach to targeted intranasal drug delivery, particularly in neurological conditions. Further experimental, pharmacokinetic, and clinical research using advanced imaging and tracing techniques may help validate these mechanisms more precisely and establish stronger scientific evidence for Ayurvedic nasal therapies. The integration of traditional Ayurvedic knowledge with contemporary biomedical and pharmaceutical sciences may open promising avenues for the development of innovative brain-targeted therapeutic strategies in the future.

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