Review Article

Exploration of Nasal Drug Delivery Approach indicated in Unani System of Medicine

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ABSTRACT

Introduction: Unani medicine is a holistic and natural healing system based on the time tested and clinically validated remedies and regimens. These haveevolved into a scientific discipline over the time, particularly in India. Intranasal drug delivery plays a pivotal role in this system, offering rapid and non-invasive drug absorption, making it especially suitable for systemic or central nervous system effects. This approach is highly favoured in the treatment of neurological disorders within Unani medicine, where convulsions are attributed to brain vessel obstructions. Various nasal dosage forms are documented, each serving distinct clinical purposes. **Objectives:** This review explores nasal drug delivery in Unani medicine, focusing on diverse dosage forms for different clinical conditions. **Methods:** The study relies on exploring Unani manuscripts, including official and non-official pharmacopoeias. **Result:** Nasal dosage forms in Unani medicine encompass solid, liquid, and gaseous formulations, each serving specific therapeutic purposes. However, classical texts lack specifics on particle size standards for nasal drug administration .**Conclusion:** The rapid and non-invasive drug absorption offered by intranasal delivery holds promise, particularly for systemic and central nervous system effects. Unani medicine prioritizes this method for managing neurological disorders, attributing convulsions to obstructions in cerebral blood vessels.

Key words: Unani Medicine, Intranasal Drug Delivery, Nasal Dosage Forms, Neurological Disorders, Traditional Medicine.

The Unani Medicine is one of the AYUSH systems of healthcare that constitutes the primary healthcare structure of India. Though the system is indeed named after the ancient Greek culture ("Unan" being the Greek name) [1]. Many researchers and historians suggest that this medical system is an evolved form of healthcare that likely originated in some of the earliest human civilizations. Its roots might even stretch back to the ancient Mesopotamian or Egyptian civilizations.Over countless generations, this medical system has thrived across diverse geographical landscapes, spanning regions from Greece, Iran, the Middle East, to Southeast Asia [1]. In the contemporary era, Unani Medicine has matured into a fully-fledged scientific discipline in the domain of healthcare and healing, with India serving as a prominent epicentre of this pathy [**2**]. Unani medicines are sourced from three primary natural reservoirs, namely plants, animals, and minerals. These substances are conventionally administered via oral and few other routes. Among these routes, one notable method of drug administration is the intranasal drug delivery system [**3**].

Nasal drug delivery system is a novel and promising route for delivering drugs to the systemic circulation or the central nervous system. It has many advantages over oral or parenteral administration, such as rapid and high bioavailability, avoidance of first-pass metabolism, non-invasiveness, and ease of administration [4]. However, it also faces some challenges and limitations, such as low permeability for some drugs, mucociliary clearance, enzymatic degradation, and variability in absorption [5]. Therefore, it is important to design and optimize nasal drug delivery systems that can overcome these barriers and ensure safety and stability of the drugs [5,6].

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According to Unani Medicine principles, the nasal route is employed for both systemic of local drug effects and Classical manuscripts provide substantial evidence of its extensive use in Unani Medicine, particularly as a vital route for drug delivery, especially in the treatment of neurological disorders such as epilepsy and convulsions. The rationale behind the use of the intranasal route for drug delivery in neurological disorders is based on the Unani belief that convulsions arise from obstructions in the vessels of the brain. To alleviate these obstructions, the intranasal route is favoured due to its proximity to the brain [**7**].

Unani Medicine has documented various dosage forms under the nasal drug delivery system. Consequently, this paper provides a concise exploration of the different types of nasal applications identified in Unani Medicine, along with their therapeutic indications. This examination aims to enhance our understanding of the pharmaceutical and clinical knowledge held by Unani Physicians. Moreover, this review is expected to facilitate the development of suitable herbal intranasal formulations to achieve specific therapeutic objectives. In light of the information gained, various types of herbal nasal drug formulations can be developed, including nasal drops, nasal sprays, nasal gels, nasal suspensions and emulsions, and nasal powders, among others. Thus the objective of the present study was to explore the composite nasal drug delivery system indicated in the Unani system of medicine along with the various nasal dosage forms used in different clinical conditions.

MATERIALS AND METHOD

The study of the present paper is centred on the exploration of the classical manuscripts of Unani Medicine commonly referred as "Qarabadeens" or "Unani Pharmacopoeias". Pharmacopoeia has a detailed description of the ingredients and the preparation procedure of the formulations. There are 14 official Pharmacopoeias of Unani Medicine in India recognised under the First Schedule of the Drug & Cosmetic Act, 1940.In current study, both official and non-official pharmacopoeias of Unani Medicine were studied to derive the various dosage forms related to nasal drug delivery along with their therapeutic indications.

RESULT

The nasal drug delivery system offers a wude range of dosage forms like:

1. **Inhalation:** shamum, lakhlakha,
2. **Vapour bath:** inkibab
3. **Nasl snuffing drops:** sa'ut
4. **Nasal Drops:** Qaṭūr-i-Anf
5. **Aromatic powder:** Ghaliya
6. **Liquid Snuff:** Nashūq
7. **Snuff:** 'Aṭūs
8. **Insufflation:** Nafukh
9. **Fumigation:** Bakhūr/Dhūnī

These provide stimulation of the nerves and brain, alleviation of mood,decongesion of the respiratory passage,soothing of the irritated mucosa,evacuation of the morbid material, vasoconstriction,muscle relaxation and antispasmodic activity. The observations made by the authors are presented in the table given below:

Table 1: Various Nasal Drug Delivery Systems in Unani Medicine: Their Indications, Method of Preparation and Mode of Action

Dosage Form	Definition	Indications	Method of preparation [9]	Mode of Action [17]
Shamūm (Inhalation)	Inhalation of drugs which may be in dry or liquid form so that volatile substances reach nasal cavity and respiratory tubes [8]	Headache, Migraine, Hemiplegia, Facial Palsy, Apoplexy, Brain Tonic, Vertigo [10,11,12,15,16]	Desired drugs are pounded in a mortar and put in a tenuous cloth to be smelled by patient 3-4 times a day.	Stimulation of Nerves and Brain, Alleviation of mood, Exhilarant
Lakhlakha (Inhalation)	The inhalation of the vapours from drugs kept in a wide mouthed bottle [8]	Headache, Meningitis, Palpitations, Cardio Tonic, Insomnia [11,13,14,15]	Desired herbs are pounded with a suitable extract and kept in wide mouthed bottle for inhalation.	Stimulation of Nerves and Brain, Alleviation of mood, Exhilarant
Inkibab (Vapour Bath)	The exposure of a part of the body or the whole body to the vapours obtained from the	Headache, Meningitis, Insomnia, Vertigo, Coryza and Catarrh, Asthma, Bronchitis [10,14,15]	Desired Drugs are boiled in water and the resultant steam is then inhaled.	Decongestion of respiratory passages, soothing of irritated and inflamed mucous membranes in the throat and airways, humidification,

	decoction of drugs or boiled simple water [8]			evacuation of morbid matter through sweat, regulate blood circulation, muscle relaxation
Sa'ut (Nasal Snuffing Drops)	A liquid preparation which is sniffed in the form of drops.	Epistaxis, Diphtheria, Nasal Polyps, Headache, Migraine, Meningitis, Melancholia, Epilepsy, Vertigo, Hemiplegia, Facial Palsy [14,15]	Desired drugs are taken in required quantity, pounded finely and mixed with a Distilled water or extract of suitable drugs and the drops are instilled in nose.	Evacuation of morbid material and stimulation of nerves and brain
Qaṭūr-i-Anf (Nasal Drops)	Liquid drug taken in doses measured by drops and used in different nasal ailments [8]	Epistaxis, Diphtheria, Nasal Polyps, Headache, Migraine [10,11]	Desired medicinal herbs either in the powder or paste form are added to the base oil or extract of medicine or kept for several days, this is then strained through muslin cloth or strainer and kept in an airtight container.	Vasoconstriction, anti-inflammatory, decongestion, stimulation
Ghāliya (Aromatic powder/ Perfumed powder)	Aromatic powder, prepared from specific aromatic herbs for local application [8]	Brain Tonic, Cardio Tonic, Palpitations[13,14]	Desired drugs are pounded with pestle and mortar into a fine powder which is strained through fine muslin cloth and kept in an airtight container.	Nerve stimulation, Exhilarant
Nashūq (Liquid Snuff)	Liquid preparation used for snuffing [8]	Headache, Meningitis, Apoplexy, Deobstruent [14,15]	It is prepared in the same way as Sa'ut, but the difference is that patient himself/ herself inhale the droplets of drug.	Stimulation of brain and nerves, regulationof temperament
'Aṭūs (Snuff)	A finely powdered drug that is inhaled to induce sneezing[8]	Phlegmatic Headache, Amnesia, Epilepsy, Hemiplegia, Phlegmatic Diseases of Brain, Cleansing of Brain [10,14,15]	Desired drugs are grinded, blended, or processed into either liquid or dry form.	Evacuation of morbid material and stimulation of nerves and brain,
Nafūkh (Insufflation)	Finely powdered drug that is blown with the help of a tube in nose, throat or any other opening of the body [8]	Epistaxis, Ozaena, Nasal Mucosal Hypertrophy, Nasal Obstructions, Headache, Migraine, Epilepsy, Apoplexy, Hemiplegia, Cleansing of Brain, Catarrh [11, 14,15]	Desired drugs are pounded to a very fine powder and a low dose of drugs around 20 mg is blown into both nostrils of patient with the help of some straw.	Evacuation of morbid material and stimulation of nerves and brain
Bakhūr/Dhūnī (Fumigation)	Inhalation of fumes produced by burning of either single or compound drugs on the flame so that vapoursreach the brain or smoking an affected organ by burning the drugs [8]	Headache, Meningitis, Convulsions, Hemiplegia, Phlegmatic Cough, Bronchial Asthma, Haemoptysis, Syncope [14,15,16]	Desired herbs are grounded or crushedinto fine powder or small pieces. Which is then sprinkled over a burning piece of charcoal tablet. The fragrant smoke is then inhaled.	Evacuation of morbid material and stimulation of nerves and brain, Decongestion of respiratory passages, muscle relaxation, anti-spasmodic effect

DISCUSSION

The preceding observations unequivocally demonstrate the diverse array of nasal dosage forms available in Unani system of Medicine. These dosage forms can be categorized into three primary groups based on their physical states, namely solid, liquid, and gaseous formulations. Solid dosage forms encompass drug powders administered

through nasal insufflation (*Nafūkh*) and snuff *(Aṭūs*). Liquid formulations include solutions and liquids, such as nasal drops (*Qaṭūr-i-Anf*), nasal snuffing drops (*Sa'ut*), and liquid snuff formulations (*Nashūq*). Gaseous preparations encompass fumigations (*Bakhūr*), steam or medicinal vapour baths (*Inkibab*), inhalation forms (*Lakhlakha*), and aromatic sprinkling powders (*Ghāliya*), where aromas are inhaled through the nasal passage. Furthermore, we must not overlook the mention of *Shamūm*(Inhalation), which entails the inhalation of drugs in both dry and liquid forms, allowing volatile substances to reach the nasal cavity and respiratory passages—an aspect worthy of pharmacological investigation [8].

When we studied the classical texts of Unani medicine for reference of nasal drugs, we observed that the drugs intended for use as *'Aṭūs* (snuff) and *Nafūkh* (insufflation) are solid dosage forms and prepared as microfine powders [9]. This observation lends itself to the deduction that whether these agents are administered in a liquid or solid state, the initial step involves the preparation of a microfine powder comprising the desired medicinal substances. Subsequently, when the liquid form is preferred, this powder is blended with suitable distillate. It indicates that the Unani physicians recognized the importance of reducing particle size for effective nasal insufflation [10]. When we considered the gaseous dosage forms such as *Bakhūr/Dhūnī* (fumigation) and *Inkibab* (vapour bathes), which were more intended for respiratory diseases such as bronchitis, bronchial asthma, cough etc, the desired herbs are first grounded or crushed into fine powder or small pieces and then sprinkled over a burning piece of charcoal tablet for inhaling the smoke is then inhaled in case of fumigation therapy. For *Inkibab* (vapour bathes), the desired drugs are first crushed and pounded and then boiled in water and the resultant steam is then inhaled [11].

According to contemporary pharmaceutical research, particles or droplets that are larger than 10 μm in diameter are more likely to be retained in the nasal cavity and not enter the lungs upon inhalation [18,19]. This particle size is desirable for drugs that aim for local or systemic effects through the nasal mucosa. Some studies also suggested that larger particles may also have lower bioavailability and higher clearance rates than smaller particles, as they may be subject to mucociliary clearance or enzymatic degradation [20]. Therefore, it is believed that particles in the range of 10–50 μm are optimal for nasal drug delivery, as they can achieve a balance between retention and absorption [21].

For particles or droplets that are smaller than 10 μm in diameter are more likely to reach the lower respiratory tract and the alveoli, where they can have systemic effects or target the lung tissue [22]. This is desirable for drugs that aim for systemic absorption or local effects in the lungs. However, smaller particles may also have lower deposition efficiency and higher exhalation rates than larger particles, as they may follow the airstream and not impact on the airway walls. Therefore, studies suggest that particles in the range of 1–5 μm are optimal for fumigation or inhalation therapy, as they can achieve a balance between penetration and deposition [22].

However, we could not find any prescribed standardof the particle size of drugs intended to be use through nasal route in Unani system of Medicine. According to the Unani Pharmacopoeia of India, the particle size of fine powders is defined as the one that passes through a sieve with a nominal mesh aperture of 180 μm (Sieve No. 85) and very fine powders are those that pass through a sieve with a nominal mesh aperture of 125 μm (Sieve No. 120) [22].

According to the classical text examined in the context of this study, the therapeutic indications for Nafukh (Insufflation) encompass a spectrum of medical conditions, including Epistaxis, Ozaena, Nasal Mucosal Hypertrophy, Nasal Obstructions, Headache, Migraine, Epilepsy, Apoplexy, Hemiplegia, Brain Cleansing, Catarrh, among other [10,15,16]. On the other hand, Atus (Errhine) is indicated for the treatment of Phlegmatic Headache, Amnesia, Epilepsy, Hemiplegia, Phlegmatic Brain Disorders, and Brain Cleansing [15]. The text suggests that the probable mode of action of these therapies is multifaceted, contingent upon the intended systemic or local effects. When a systemic effect is sought, the mechanisms involve the evacuation of disease-causing agents and the stimulation of nerves and brain functions. Conversely, for local effects, the actions include decongestion of respiratory passages, soothing of irritated and inflamed mucous membranes in the throat and airways, humidification, elimination of pathological substances through perspiration, regulation of blood circulation, and muscle relaxation [17].

CONCLUSION

In accordance with the principles of the Unani system of Medicine, the nasal route of drug delivery serves as a vital strategy for the management of a wide spectrum of systemic and localized ailments. As the nasasl drug delivery system bpasses the hepatic first pass metabolism it offers a quick relief. Hence it is particularly of great importance in treating acute exacerbations of the ailments.

Nevertheless, the realization of this innovative drug delivery approach within the framework of Unani medicine demands rigorous exploration of mechanistic intricacies,

procedural standardization, formulation optimization, and the implementation of robust quality control measures. Only through such comprehensive endeavours can the full potential of this novel drug delivery technique be harnessed for optimal patient care.

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