

BEYOND THE ORAL ROUTE: A COMPREHENSIVE REVIEW ON TRANSMUCOSAL AND TARGET-SPECIFIC DRUG DELIVERY IN CLASSICAL *VISHA* *CHIKITSA*

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Abstract

Background: Traditional Ayurvedic pharmaceuticals relies heavily on the oral route for systemic drug delivery. However, in emergency toxicology (*Visha Chikitsa*), the oral route presents severe limitations, including delayed onset of action, destruction by digestive juices, and first-pass hepatic metabolism. Crucially, it becomes completely unviable when a patient presents with unconsciousness, or severe gastrointestinal distress such as vomiting and diarrhoea. To bypass these barriers, alternative routes like trans-nasal (*Nasya*) and trans-ocular (*Anjana*, *Aschyotana*) administration are prioritized in acute poisoning cases to facilitate rapid, direct-to-site therapeutic action.

Objective: This review compiles and evaluates the anatomical, physiological, and pharmacokinetic bases of trans-nasal and trans-ocular drug delivery systems as described in classical Ayurvedic toxicology and validated by contemporary biopharmaceutics.

Methods: A narrative literature review was undertaken using classical Ayurvedic texts, including the *Charaka Samhita*, *Sushruta Samhita*, *Ashtanga Samgraha*, and *Visha Vaidya Jyotsnika*, to identify references related to *Nasya*, *Anjana*, and *Aschyotana* in *Visha Chikitsa*. Contemporary evidence was retrieved from PubMed, Scopus, and Google Scholar using terms related to intranasal and ocular drug delivery, nose-to-brain transport, blood–brain barrier bypass, mucosal absorption, ocular permeability, pharmacokinetics, and nano formulations. Relevant evidence was critically compared with classical descriptions and synthesized narratively to evaluate the scientific basis and potential application of these routes in emergency toxicology

Results: The nasal mucosa's rich vascularization and direct access to the olfactory and trigeminal nerve pathways allow *Nasya* to bypass the blood-brain barrier (BBB), thereby potentially facilitating rapid restoration of consciousness. Similarly, ocular delivery via *Anjana* utilizes the conjunctival and scleral pathways for fast systemic and local action via the *Shiro-Marma*. Modern formulations like piperine-loaded mucoadhesive nano emulsions mirror the enhanced bioavailability principles seen in traditional *Sasukshma Pishta* (ultra-fine) preparations like *Vilwadi Churna* and *Mrityunjaya Anjanam*.

Conclusion: Transnasal and transocular routes provide rapid, non-invasive, targeted drug delivery essential for emergency integrative toxicology.

Keywords: *Visha Chikitsa*, *Nasya*, *Anjana*, Nose-to-Brain Delivery, Trans-mucosal, Piperine Nanoemulsion.

Introduction

Ayurvedic therapeutics has traditionally leaned on oral drug administration for treating systemic illnesses. However, in the realm of *Visha Chikitsa* (Ayurvedic clinical toxicology), relying strictly on oral drug delivery poses an existential threat to patient survival. Envenomation and poisoning are medical emergencies where there is no time to spare. The conventional oral route exhibits several systemic drawbacks that render them obsolete during acute crises: delayed onset of action due to gastrointestinal transit times, unsuitability for

irritant or highly unpalatable formulations, destruction of active phytoconstituents by harsh gastric juices, and significant drug inactivation via the hepatic first-pass effect^[1] Furthermore, clinical presentations of acute poisoning frequently include complications like continuous vomiting, severe diarrhoea, or total unconsciousness, which physically preclude oral administration

To manage these life-threatening situations, ancient Ayurvedic *Vaidyas* developed specialized clinical interventions within the *Chaturvimshati Upakrama* (24 therapeutic steps for managing poison). Among these, transnasal (*Nasya*) and transocular (*Anjana*, *Aschyotana*) drug delivery stand out as premier non-oral pathways.

The nasal cavity provides a unique gateway because of its highly ramified network of blood capillaries and close proximity to the central nervous system. Administering medicines via the nostrils directly stimulates brain centres compromised by the toxic properties (*Madakaari Guna*) of a poison, facilitating an instantaneous return to consciousness. Simultaneously, the ocular route capitalizes on the highly permeable trans-conjunctival tissue layer to deliver low-dose, high-potency *Vishaghna* (anti-toxic) compounds directly into the systemic circulation and surrounding cranial structures.

This review correlates these classical Ayurvedic methodologies with modern anatomical, physiological, and pharmacokinetic insights, demonstrating that ancient emergency therapies align with advanced drug delivery concepts like nose-to-brain targeting and trans-mucosal macromolecular absorption^[2]

Materials and Methods

The review involved a comparative analysis across two primary domains:

1. **Ayurvedic Textual Source Evaluation:** Traditional literature regarding the utility, preparation, dosage, and indications of *Nasya* (nasal therapy) and *Anjana* (ocular collyrium) was parsed from the *Brihatrayi* (*Charaka Samhita*, *Sushruta Samhita*, and *Ashtanga Sangraha/Hridaya*). Special focus was placed on the specific placement of these therapies within the *Chaturvimshati Upakrama*. Additionally, regional toxicological literature specifically the *Visha Vaidya Jyotsnika* was reviewed to analyse classical multi-ingredient formulations like *Mrityunjaya Anjanam*, *Garudanjanam*, and *Dasabeejanjanam*.
2. **Modern Pharmaceutical Literature Integration:** Contemporary biopharmaceutical datasets were reviewed to isolate the physical, anatomical, and chemical parameters governing nasal and ocular absorption. This included an analysis of human nasal anatomy metrics (surface area, volume, regional divisions), paracellular vs. transcellular diffusion mechanisms, precorneal loss factors, and advanced nanotechnology-driven delivery vehicles (such as mucoadhesive nano emulsions engineered for enhanced bioavailability of *Maricha* derivatives like piperine)

1.Nasya karma.

Ayurvedic Perspective of Trans-Nasal Drug Delivery (*Nasya Karma*) In classical Ayurveda, *Nasa* (the nose) is recognized as the definitive gateway to the head (*Nasaa hi shiraso dvaram*). Medicines introduced through the nasal passage travel throughout the cranial vault, systematically eliminating or neutralizing localized morbid Doshas responsible for systemic pathology.

1.1 Classification and Indications in toxicology

While *Nasya* encompasses wide-ranging applications in general medicine, its structural adjustments under *Visha Chikitsa* centre around immediate bio-availability and emergency detoxification^[3]. The primary clinical variants utilized include:

1. **Shodhana Nasya (Cleansing/Evacuating):** Employed for the aggressive expulsion of localized toxins and accumulated morbid factors in the head region.
2. **Shamana Nasya (Palliative/Calming):** Designed to pacify the acute, spreading neurotoxic effects triggered by envenomation.
3. **Marshya nasya and Pratimarsha Nasya:** Selected based on dose adjustments for ongoing tissue nourishment or management of chronic, low-grade toxic exposure.

Nasya Karma is uniquely practical in emergency medicine because it bypasses the mandatory pre-therapeutic regimens of *Snehana* (internal/external oleation) and *Swedana* (sudation) required by systemic purificatory therapies like *Vamana* (emesis) or *O* (purgation). It is indicated for both inanimate (*Sthavara*

Visha) and animate (*Jangama Visha*) poisonings, including snakebites (*Sarpa Damsha*), rodent bites (*Mooshaka Visha*), spider envenomation (*Loota Visha*), insect stings, and artificial/chemically induced combinations (*Gara Visha*). It is specifically mandated as the primary treatment whenever toxic features manifest in the head (*Shirogata Visha*).

1.2 Key Modes of Administration & Dosage Parameters

I. *Avapida Nasya*

Avapida denotes the mechanical expression of fresh liquid juice from crushed medicinal leaves or a prepared herbal paste (*Kalka*). In the context of *Vishaabhighaata* (acute toxic injury), it functions primarily as a powerful *Shodhana* (purificatory) intervention. Highly potent, irritating, and penetrating (*Tikshna*) herbs such as *Saindhava* (rock salt) and *Pippali* (*Piper longum*) are crushed into pastes to make the nasal drops [4]. The dosage strictly mimics *Shirovirechana* standards to prompt rapid upper-airway evacuation:

- *Hina Maatraa* (Minimum Dose): 4 drops per nostril.
- *Madhyama Maatraa* (Medium Dose): 6 drops per nostril.
- *Uttama Maatraa* (Maximum Dose): 8 drops per nostril.

II. *Dhmaapana / Pradhamana Nasya*

Dhmaapana (as named in the *Charaka Samhita*) or *Pradhamana* (per the *Sushruta Samhita*) is a highly specialized dry-powder inhalation strategy described as 13th among the *Chaturvimshati Upakrama*

1. Basic Principle

Fine medicated powder blown into the nasal passage spreads rapidly across the respiratory tract, physically confronting and limiting the systemic spread of the circulating poison.

2. Primary Herbs

Tikshna drugs: *Katukaa*, *Katabhi*, *Katphala*, *Maricha*, *Garlic*, *Guggulu*, and *Saindhava*.

3. Mechanical Devices

Administered using a *Naadi Yantra* a customized, straight, open-ended tube measuring 6 *Angulas* in length. The powder is loaded at one tip, placed inside the nostril, and forcefully blown into the airway from the opposite end.

4. Alternative Method (*Videha*)

Acharya *Videha* detailed an alternative method utilizing a *Pottali* (a small sachet made of porous, thin cloth) packed with fine powder, which is placed over the nose for direct inhalation of microscopic herbal particles.

5. Standard Dosage

3 *Muchuti* (3 pinches) when utilizing the direct blowing technique. For the cloth *Pottali* technique, a minimum powder mass of 2 *Tolas* (approx. 20 grams) must be utilized to maintain adequate particulate pressure.

III. *Dhooma Pana / Dhuma Nasya*

Dhoomapana refers to the controlled inhalation of anti-toxic, medicated smoke generated by burning specialized formulations. It occupies the 17th rank within the *Chaturvinshati Upakrama*. The entering therapeutic fumes physically cleanse all micro-channels of circulation (*Strotasa*), instantly clearing organic obstructions and neutralizing systemic toxic residues.

Strict administrative boundaries apply: true *Dhuma Nasya* requires the medicated smoke to enter via the nasal passage and exit exclusively via the oral cavity. Oral-inbound smoking (*Doomapana*) is distinctly classified apart from *Nasya* and is warned against in emergency toxidromes due to its damaging effect on visual acuity (*Netra Hani*).

The clinical forms include:

- *Praayogika Dhuma* (Routine/General anti-toxic): Formulated with aromatic, stabilizing herbs like *Priyangu* and *Ushira*.
- *Snaihika Dhuma* (Lubricating/Demulcent): Formulated with soothing bases like *Vasaa* and *Ghrita* (clarified butter) to counter dry, neurotoxic venoms.
- *Vairechanika Dhuma* (Purgative/Evacuating): Utilizes strong, irritant plants like *Aparajitaa* and *Apamaarga* to clear deep, unresponsive comatose conditions

1.3 Modern Pharmacological and Biophysical Basis of Nasal Absorption

Modern biopharmaceutics validates the ancient preference for the nasal pathway in emergency crises. The human nasal cavity presents a highly vascularized mucosal architecture with a total working volume of approximately 16 to 19 mL (split evenly to about 7.5 mL per cavity by the central nasal septum) and an expansive surface area of 180 cm² (75 cm² per cavity) [5]. When a drug is delivered into this space, it deposits across three distinct zones: the vestibular, the respiratory, and the olfactory regions

a) Anatomical Pathways to the Central Nervous System

Trans-mucosal nasal administration offers distinct advantages when intravenous, intramuscular, or oral pathways are structurally blocked or delayed. It exhibits superior systemic bioavailability for large molecules, proteins, and peptides compared to oral pathways due to the absolute lack of pancreatic and gastric enzymatic degradation, a neutral mucosal pH environment, and the circumvention of hepatic first-pass extraction. Drugs penetrate the mucosal boundary via two primary transport mechanisms:

b) The Aqueous / Paracellular Route:

A passive transport mechanism where water-soluble drugs slip through the narrow intercellular spaces between adjacent epithelial cells. This pathway shows a strict inverse log-log correlation with molecular weight; compounds exceeding 1000 Daltons demonstrate poor bioavailability. To counter this limitation, ancient texts mandate grinding emergency mixtures into an ultra-fine state (*Sasukshma Pishta*), a practice explicitly seen in formulations like *Vilwadi Churna* to enhance surface area and optimize paracellular transit.

c) The Lipoidal / Transcellular Route:

A highly efficient, rate-dependent diffusion process utilized by lipophilic agents to pass directly through the lipid bilayer of epithelial cell membranes. This route utilizes carrier-mediated active transport or transient openings within cellular tight junctions.

d) Bypassing the Blood-Brain Barrier (BBB)

The clinical capacity of *Nasya* to treat comatose states stems from two anatomical pathways that permit direct nose-to-brain delivery, completely bypassing the selective Blood-Brain Barrier (BBB):

- **Olfactory Nerve Pathway:** Axons of the olfactory receptor cells project directly from the nasal cavity's upper vault through the cribriform plate into the olfactory bulb of the brain. This provides a direct fluid pathway for lipophilic molecules into the central nervous system.
- **Trigeminal Nerve Pathway:** Branches of the trigeminal nerve vascularize the respiratory and olfactory mucosa, creating a secondary entry point into the pons and brainstem structures.

In acute toxicity, this neural access is vital. Strong (*Tikshna*) formulations cause localized mucosal irritation, triggering a rapid reflex activation of cranial nerves (CN V, VII, IX, and X). This neuro-stimulation reactivates depressed brainstem centres, improving breathing rhythms and restoring consciousness. Modern critical care utilizes this exact pathway for the delivery of emergency agents like naloxone (opioid antidote), anti-migraine medications, and fast-acting anti-epileptics.

1.4 Advanced Pharmaceutical Validation: The Piperine Model

The traditional reliance on *Purana Maricha* (aged black pepper) in emergency *Nasya* is supported by contemporary nano-formulation research. *Maricha's* primary alkaloid, piperine, is highly lipophilic, enabling it to diffuse across the nasal epithelium and cross the BBB with ease.

By introducing the formulation directly into the nostrils, the medicine completely bypasses the gastrointestinal tract, protecting vulnerable active ingredients from degradation by harsh gastric juices and avoiding the liver's delayed first-pass metabolism. Once deposited onto the nasal cavity mucosa, the highly lipophilic piperine molecule easily passes through the thin epithelial layer via rapid paracellular and transcellular absorption pathways. From here, the drug acts through two simultaneous mechanisms [6]: it triggers local mucosal irritation that provides direct olfactory and trigeminal nerve neuro-stimulation to reactivate depressed central nervous system (CNS) brainstem centres, while concurrently getting absorbed into the local capillary network. As piperine enters the systemic circulation and crosses the blood-brain barrier (BBB), it exerts a strong bio-enhancing effect by systematically inhibiting hepatic/intestinal glucuronidation and suppressing defensive P-glycoprotein efflux pumps at the BBB. This cellular lockdown prevents the brain and body from expelling therapeutic agents, drastically boosting the systemic bioavailability, speed, and sustained action of co-administered anti-toxic herbs, such as those found in *Vilwadi Churna*.

Consequently, when *Maricha* is added to complex formulas like *Vilwadi Churna*, it stops the brain from pumping out therapeutic compounds, ensuring a sustained antitoxic effect. Recent pharmaceutical studies have successfully engineered stable mucoadhesive nano emulsions loading isolated piperine via titration methods. These preparations feature optimized droplet scales: standard nano emulsions measure <100 nm with negative zeta potentials, while specialized mucoadhesive designs measure <150 nm with a positive zeta charge. This positive charge bonds with the negative charge of nasal mucin, extending retention time. Transmission Electron Microscopy (TEM) confirms their uniform spherical structures, and their viscosity profiles align with natural nasal fluids. In vitro evaluations demonstrate an efficient release profile, delivering over 85% of the active compound within 4 hours directly across the mucosal membrane.

2. Trans-Ocular Drug Delivery in *Visha Chikitsa*

Trans-ocular drug delivery involves administering therapeutic agents directly onto the surface of the eye to achieve localized or systemic antitoxic outcomes^[7]. In Ayurvedic toxicology, the eye is classified as an organ dominated by *Rakta* (blood) and *Alochaaka Pitta* (The fire residing in eye), making it a primary site for the accumulation and manifestation of circulating poisons.

2.1 Ocular Manifestations and Detoxification Modalities

Systemic envenomation frequently causes severe ocular symptoms, including peri-orbital oedema (*Shoonaakshikootam*), persistent sleep disturbances (*Nidra*), distinct discoloration of the sclera/conjunctiva (*Vivarna*), accumulation of toxic debris (*Aavila Lochanam*), and blurred or distorted vision.

To counter these manifestations and clear visual obstructions (*Akshyuparodham*), *Visha Chikitsa* utilizes four specific local therapies that interface with the *Shiro-Marma* network^[8]:

- ***Aschyotana* (Medicated Eye Drops):** Instilling liquid formulations directly onto the conjunctival sac for immediate capillary absorption.
- ***Anjana* (Medicated Collyrium):** Applying concentrated pastes, semi-solids, or fine powders to the lower lid margin to supply long-acting *Vishaghna* (antitoxic) compounds.
- ***Netra Tarpana* (Ocular Bathing):** Retaining a pool of warm, medicated lipid pools (*Ghrita*) over the open eye to extract lipid-soluble toxins.
- ***Putapaka*:** Applying specialized herbal extracts to rejuvenate ocular tissues after acute chemical or venom-induced injury.

2.2 Chronological Indications and Formulation Matrix

The administration of *Anjana* is meticulously synchronized with the progression of venom poisoning (*Visha Vega*):

- **Elapid snake envenomation (*Darveekara Sarpa Vega*):** Explicitly indicated during the 3rd and 7th stages of systemic poisoning to counteract advancing neuromuscular paralysis and preserve visual function.
- **Viper Envenomation (*Mandali Visha Vega*):** Mandated at the 7th stage to manage extensive systemic coagulopathic breakdowns.
- **Krait envenomation (*Rajila Visha Vega*):** Deployed at the 3rd and 6th stages to treat neuromuscular blockages.

According to the *Charaka Samhita*, the 5th *Visha Vega* requires immediate *Aschyotana* and *Anjana* prepared from the fresh expressed juice (*Swarasa*) of *Kakanda* and *Sireesha* (*Albizia lebbek*). It stands as one of the 10 vital therapies for spider bites (*Lutha Damsha*) and is used as a *Samjasthapana* (consciousness-restoring) tool across all uncommunicative, comatose patient profiles. Specific antidotes include *Hinguvachadi Gutika* for scorpion stings (*Vrishchika Visha*) and *Trikatu* processed with fresh cow dung juice (*Gomaya Swarasa*) for rodent bites (*Mushika Visha*)^[9,10,11,13]

Traditional toxicological handbooks, such as the *Visha Vaidya Jyotsnika*, emphasize three core formulations designed for patients presenting with deep unconsciousness. This preparation combines four mineral bases, three herbal components, and an organic binding substrate.

a) *Mrityunjaya anjanam*

It consists of four mineral drugs, three herbal drugs and eggs of ant. The mineral drugs are *Tuttha* (Copper sulphate), *Gandhaka* (Sulphur), *Parada* (Mercury), *Sasyaka* (Copper sulphate). The herbal drugs are Swetha gunja (*Abrus precatorius*), *Purana mulaku* (*Capsicum annum*) and *Bakula* (*Mimusops elengi*)^[14]

b) *Garudanjanam*

A complex preparation combining seven minerals and seven herbs:

- **Minerals:** *Anjana* (Stibnite), *Saindhava Lavana* (Rock salt), *Tuttha*, *Tankana* (Borax), *Parada*, *Tamra* (Purified Copper), and *Shankha* (Calcium carbonate).
- **Herbs:** *Shunti* (*Zingiber officinale*), *Maricha*, *Pippali*, *Nili* (*Indigofera tinctoria*), *Nagadanti* (*Baliospermum montanum*), *Shigru* (*Moringa oleifera*), and *Jambeera* (*Citrus limon*) juice.

Actions: The minerals provide sustained chemical defence against venom enzymes, while *Nagadanti* and *Nili* offer systemic *Vishaghna* (anti-poison) properties ^[15]

c) *Dasabeejanam*

Utilizes four mineral ingredients *Tuttha*, *Tankana*, *Anjana*, and *Saindhava Lavana* processed alongside ten distinct herbal seeds and extracts: *Neeli*, *Tulasi* (*Ocimum sanctum*), *Danti*, *Shigru*, *Nimba* (*Azadirachta indica*), *Shireesha*, *Maricha*, *Bakula*, and *Gunja*. This formulation specializes in reversing advanced neurotoxic coma by stimulating cranial nerve endings around the orbits ^[16].

Table no.1 Describe properties of different ingredients helps in Trans ocular drug absorption

Component Classification	Ingredients	Pharmacological Profile (<i>Rasa, Guna, Veerya, Vipaka</i>) & Therapeutic Actions (<i>Karma</i>)
Mineral Ingredients	<i>Tuttha</i> (Copper sulphate), <i>Gandhaka</i> (Pure Sulphur), <i>Parada</i> (Purified Mercury), <i>Sasyaka</i> (Copper sulphate variant).	• <i>Tuttha/Sasyaka</i>: Pungent, astringent, sweet, hot in potency; functions as a powerful antimicrobial (<i>Krimighna</i>) and anti-psychotic (<i>Grahaghna</i>). • <i>Gandhaka</i>: Pungent, bitter, hot in potency; acts as an intense antitoxic (<i>Vishahara</i>) and ocular rejuvenator. • <i>Parada</i>: Possesses all six tastes (<i>Shadrasa</i>), mobile, hot in potency; serves as a universal potentiator (<i>Rasayana</i>).
Herbal Ingredients	<i>Swetha Gunja</i> (<i>Abrus precatorius</i>), <i>Purana Mulaku</i> (<i>Capsicum annuum</i>), <i>Bakula</i> (<i>Mimusops elengi</i>).	• <i>Swetha Gunja</i>: Bitter, astringent, hot; improves visual acuity and neutralizes toxic fractions. • <i>Purana Mulaku</i>: Intensely pungent, dry, sharp; serves as a potent local analgesic and sensory stimulant (<i>Vedanasthapana</i>). • <i>Bakula</i>: Pungent, astringent, heavy, cold; targets systemic toxin degradation.
Organic Substrate	Eggs of Ants.	• Functions as a biochemical vehicle (<i>Anupana</i>) to optimize tissue penetration.

3. Modern Ocular Biophysics and Pharmacokinetic Mechanics

Contemporary ocular drug delivery evaluates the eye as a compartmentalized structure that absorbs drugs through topical, intraocular, or periocular pathways.^[17] Topical delivery remains the primary non-invasive clinical approach, utilizing the conjunctival capillaries for systemic entry.

3.1 Ocular Absorption Barriers and Dynamic Clearance

The efficiency of trans-ocular delivery is limited by significant physiological defence barriers:

1. **Pre-corneal Dynamic Clearance:** Standard commercial dropper units deliver volumes between 40 to 50 μ L, but the human conjunctival sac has a resting capacity of only 30 μ L. Upon blinking, this drops to a mere 10 μ L, causing a significant portion of the medicine to drain away instantly. ^[18]
2. **Anatomical Epithelial Junctions:** The corneal epithelium contains tight intercellular junctions that restrict the passive passage of large, water-soluble molecules.
3. **Surface Charge Repulsion:** At physiological pH, the corneal surface carries a net negative charge, creating an electrical barrier that repels negatively charged therapeutic ions.

4. **Tear Fluid Dynamics:** Continuous tear turnover, binding by proteins within the tear film, and metabolic degradation by localized enzymes rapidly eliminate surface-applied compounds. Radioactive tracer studies show that suspensions applied to the eye lose two-thirds of their active concentration within 2 minutes, with complete surface clearance occurring inside 15 minutes.

3.2 Pharmacokinetic Routes of Systemic Entry

When a compound escapes pre-corneal elimination, it penetrates via three primary routes:

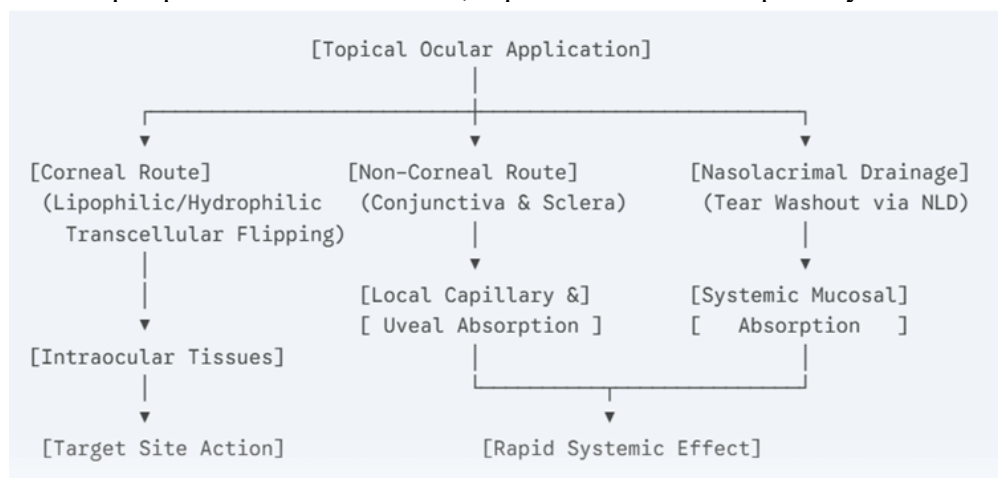


Figure- 1 Showing flow chart of trans ocular drug delivery

- **The Corneal Route:** Requires a balance of lipophilic and hydrophilic properties to cross the fat-soluble epithelium and water-soluble stroma.
- **The Non-Corneal Pathway:** ^[19] Molecules pass through the highly permeable conjunctiva and underlying sclera, allowing direct access to deeper uveal and posterior segment structures.
- **The Nasolacrimal Duct (NLD) Route:** Excess fluid drops enter the lacrimal puncta, pass through the nasolacrimal duct, and deposit along the highly vascularized nasal and pharyngeal mucosa. This mechanism facilitates rapid systemic absorption while completely avoiding hepatic first-pass metabolism.

3.3 Physical Chemistry of Ayurvedic Anjana Forms

The physical states of traditional Anjana line up closely with modern ophthalmic design categories:

- **Rasakriya Anjana (Semi-solid extracts):** Functions like clear aqueous eye drops. They dissolve completely in the tear film without sedimentation, providing rapid absorption followed by quick clearance from the conjunctival sac.
- **Gutika Anjana** (Resolidified tablets rubbed into paste) and **Churna Anjana** (Dry micro-powders): Behave like modern ophthalmic suspensions. These formulations contain micro-particulate herbal sediments that settle within the lower eyelid folds (Cul-de-sac). This particulate deposition prevents rapid washout, extends contact time with the eye, and ensures a steady release of active compound ^[20]

4. Discussion

The clinical realities of emergency toxicological management require drug delivery options that prioritize speed and reliability. While oral administration remains the standard for chronic care, its reliance during acute poisoning is limited by delayed action and physiological barriers like emesis, diarrhoea, or a complete loss of protective airway reflexes.

Trans-nasal (*Nasya*) and trans-ocular (*Anjana*) therapies solve these emergency delivery challenges. Modern anatomical mapping confirms that the nasal cavity's respiratory and olfactory zones provide unique pathways to the central nervous system. By utilizing these nerve pathways, *Nasya* can deliver low-dose, high-potency Tikshna herbs directly to the brain, bypassing the blood-brain barrier to restore consciousness in patients suffering from severe neurotoxic coma. ^[15]

Similarly, the biophysical mechanics of *Anjana* extend beyond simple localized eye care. While dynamic tear clearance and blink reflexes remove a significant portion of surface-applied liquids, the micro-particulate structures used in *Churna* and *Gutika Anjanas* bypass this limitation by depositing fine herbal particles within

the conjunctival sac. This allows for a sustained therapeutic release. Concurrently, the portion of the formula that drains through the nasolacrimal duct encounters the highly vascular mucosa of the nasopharyngeal tract, leading to rapid systemic absorption without experiencing hepatic first-pass breakdown.

Integrating these classical approaches with modern pharmaceutical technologies opens new therapeutic possibilities. For instance, combining the multi-ingredient chemistry of formulations like *Vilwadi Churna* or *Mrityunjaya Anjanam* with mucoadhesive nano emulsion bases can significantly optimize delivery performance. The use of lipophilic bio-enhancers like piperine further increases the absorption and retention of co-administered herbal compounds within the central nervous system. This convergence of traditional toxicology and modern biopharmaceutics establishes a strong foundation for developing rapid, non-invasive interventions in integrative emergency medicine.

5. Conclusion

Trans-nasal and trans-ocular drug delivery methodologies in *Ayurveda Visha Chikitsa* represent sophisticated, highly rational therapeutic systems specifically engineered for emergency medical crises. Ancient toxicologists recognized that when oral routes are blocked by coma, vomiting, or rapid systemic toxidromes, the mucosal environments of the nasal cavity and the eye offer open, highly vascular pathways for rapid drug absorption.

Modern pharmaceutical evaluations confirm that *Nasya* achieves direct nose-to-brain targeting via the olfactory and trigeminal nerve networks, bypassing the blood-brain barrier to restore critical brainstem functions. Simultaneously, *Anjana* preparations leverage particulate suspension mechanics to extend contact time on the ocular surface and facilitate systemic entry via nasolacrimal drainage channels.

Validating these traditional therapies through modern delivery systems—such as mucoadhesive nano emulsions and lipophilic piperine bio-enhancers strengthens the clinical foundation for incorporating time-tested Ayurvedic protocols into contemporary emergency care and integrative toxicology.

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