A Review on Nanoparticle-Based Nasal Drug Delivery Systems for Enhanced Brain and Systemic Delivery of Carbamazepine

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Abstract

Nasal drug delivery has gained increasing importance as a non-invasive alternative to conventional routes of administration due to its rapid onset of action, avoidance of hepatic first-pass metabolism, and potential for direct brain targeting [1,2]. Recent advancements in nanotechnology have further enhanced the applicability of the nasal route by improving drug stability, permeability, and residence time within the nasal cavity [3]. Nanoparticle-based delivery systems, particularly polymeric and lipid-based carriers, have shown promising results in enhancing the bioavailability of poorly soluble and extensively metabolized drugs [4]. This review provides a comprehensive discussion on nasal drug delivery systems with emphasis on nanoparticle-mediated approaches. Carbamazepine, a widely used antiepileptic drug with erratic oral bioavailability, is highlighted as a model drug to demonstrate the potential of nanoparticle-based nasal formulations [5].

Keywords: Nasal drug delivery, nanoparticles, chitosan, brain targeting, carbamazepine

1. Introduction

The oral route of drug administration is widely preferred due to convenience and patient compliance. However, several drugs exhibit poor therapeutic performance because of low aqueous solubility, gastrointestinal degradation, delayed onset of action, and extensive first-pass hepatic metabolism [6]. These limitations have encouraged the exploration of alternative drug delivery routes.

Among them, nasal drug delivery has emerged as a promising approach because of its highly vascularized epithelium, large absorptive surface area, and relatively high permeability [7]. In addition to systemic delivery, the nasal route provides a unique pathway for direct drug transport to the brain via the olfactory and trigeminal nerves, bypassing the blood–brain barrier [8,9]. Integration of nanotechnology with nasal drug delivery has significantly improved drug absorption and targeting efficiency [10].

2. Anatomy and Physiology of the Nasal Cavity

The nasal cavity is divided into two symmetrical chambers by the nasal septum and consists of three regions: vestibular, respiratory, and olfactory [11].

The vestibular region acts as a protective barrier against particulate matter. The respiratory region, lined with pseudostratified ciliated columnar epithelium, is the primary site for drug absorption due to its extensive surface area and rich blood supply [12]. The olfactory region contains olfactory neurons that connect directly to the brain, making it the key region for nose to-brain drug transport [13].

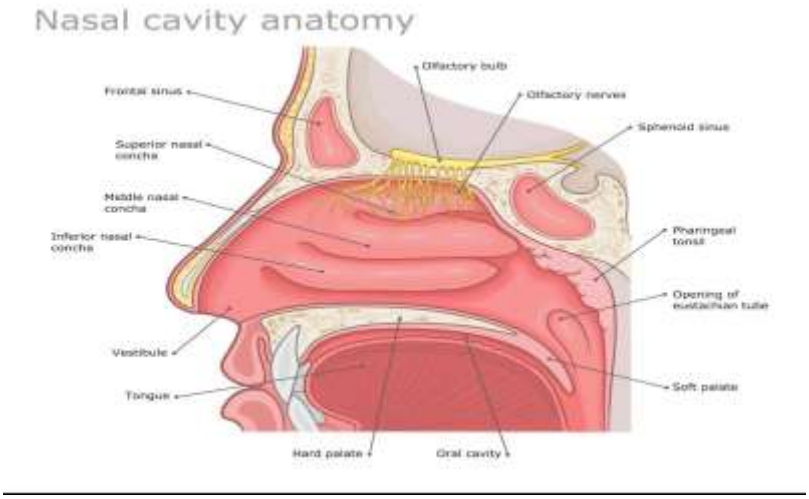

Fig. no.1 : nasal cavity anatomy

3. Nasal Mucosa and Mucociliary Clearance

The nasal mucosa consists of mucus, mucin glycoproteins, enzymes, immunoglobulins, and water [14]. Mucociliary clearance is a defense mechanism in which coordinated ciliary movement transports mucus toward the nasopharynx [15]. Although essential for nasal protection, this mechanism reduces drug residence time and limits absorption. Mucoadhesive polymers and nanoparticle-based systems are therefore employed to overcome this limitation [16].

4. Factors Influencing Nasal Drug Absorption

Nasal drug absorption is influenced by physiological factors such as blood flow, enzymatic activity, mucociliary clearance, and efflux transporters [17]. Drug-related factors including molecular weight, lipophilicity, solubility, pKa, and stability also play a crucial role [18]. Drugs with molecular weight below 1000 Da and moderate lipophilicity generally show better nasal absorption [19].

5. Advantages and Limitations of Nasal Drug Delivery

Nasal drug delivery offers advantages such as rapid onset of action, improved bioavailability, non-invasive administration, enhanced patient compliance, and potential for direct brain targeting [20]. However, limitations include restricted dosing volume, enzymatic degradation, nasal irritation, and variability in absorption [21]. These challenges necessitate advanced formulation strategies.

6. Nanoparticle-Based Nasal Drug Delivery Systems

Nanoparticles improve nasal drug delivery by protecting drugs from enzymatic degradation, enhancing mucosal adhesion, and providing controlled drug release [22].

6.1 Polymeric Nanoparticles

Chitosan-based nanoparticles are widely investigated due to their mucoadhesive properties, biocompatibility, and ability to transiently open tight junctions [23]. Nanoparticles prepared by ionic gelation using tripolyphosphate have shown improved drug entrapment and sustained release [24].

6.2 Lipid-Based Nanoparticles

Solid lipid nanoparticles and lipid–drug conjugates offer improved stability, controlled release, and enhanced brain uptake [25]. Surface modification with surfactants or PEG further enhances nasal absorption [26].

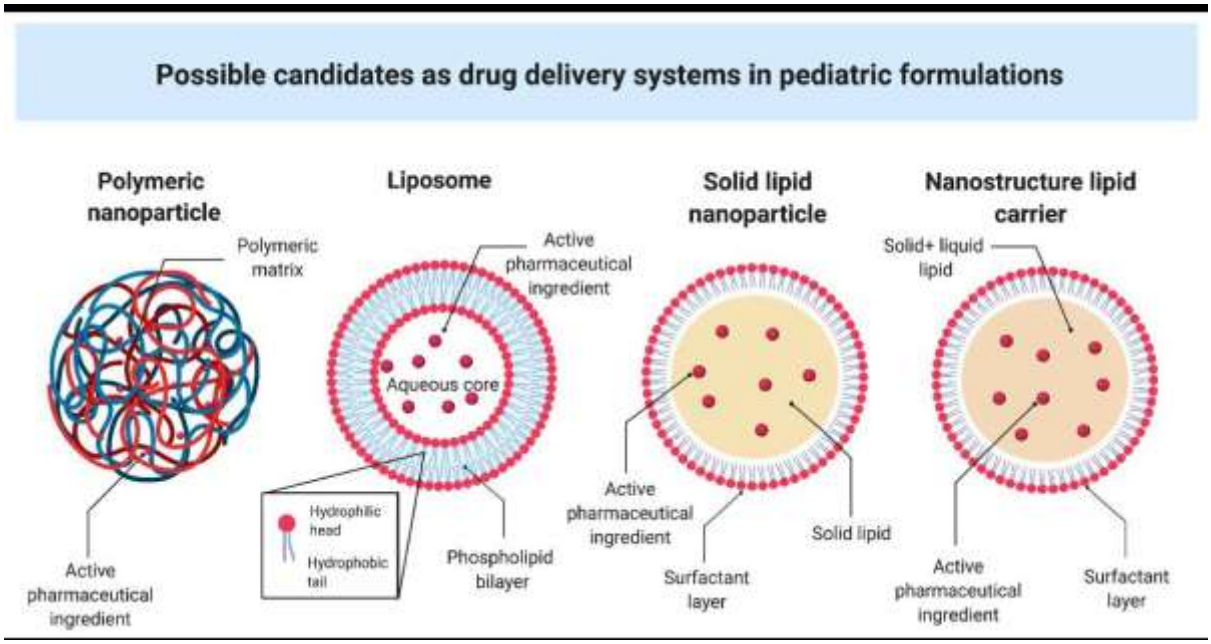

Fig.no.2: high-level overview of nasal drug delivery and brain targeting.

7. Carbamazepine as a Model Drug

Carbamazepine is a first-line antiepileptic drug used for partial and generalized seizures [27]. Despite its efficacy, oral carbamazepine exhibits slow and variable absorption, extensive hepatic metabolism, and auto-induction of metabolic enzymes [28]. These limitations make it an ideal candidate for nasal nanoparticle-based delivery.

Studies have demonstrated that chitosan-based carbamazepine nanoparticles exhibit favorable particle size, positive zeta potential, improved drug entrapment, and sustained release behavior, indicating their suitability for nasal administration [29].

Table no. 1.

Parameter	**Conventional oral formulation**	**Nasal nanoparticles**
Bioavailability	Low	Enhanced
Onset of action	Delayed	Rapid
Brain targeting	No	Yes
Dose requirement	High	Reduced
Side effects	More	Reduced
Plasma fluctuation	High	Controlled

8. Evaluation of Nasal Nanoparticles

Key evaluation parameters include particle size distribution, polydispersity index, zeta potential, drug entrapment efficiency, in-vitro drug release, and drug–excipient compatibility [30]. These parameters are essential for predicting in-vivo performance and formulation stability.

9. Future Perspectives

Nasal nanoparticle-based drug delivery systems hold significant potential for treating neurological disorders and systemic diseases. Advances in polymer science, surface modification, and formulation techniques are expected to further enhance clinical applicability [31].

10. Conclusion

Nasal drug delivery represents a promising alternative to conventional administration routes. Nanoparticle-based systems effectively address the physiological and formulation challenges associated with nasal delivery. The application of such systems for carbamazepine

demonstrates the potential to enhance bioavailability, reduce dose variability, and improve therapeutic outcomes.

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