

Formulation strategy and optimization of cinnarizine - encapsulated microspheres

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Abstract

Cinnarizine is an active histamine analog primarily used in the treatment of vertigo, tinnitus, and Meniere's disease—conditions related to vestibular disorders and inner ear dysfunction. However, Cinnarizine's clinical efficacy is hindered by its short half-life, rapid clearance, and limited oral bioavailability. Polymeric microspheres, especially those made from biodegradable materials such as Poly (lactic-co-glycolic acid) (PLGA) and Chitosan, have shown considerable potential for controlled drug release. The current research work focused on the preparation and optimization of Cinnarizine microspheres, which can be scaled up and used commercially in future.

Keywords: PLGA, Chitosan, Microspheres, solvent evaporation.

1. Introduction

This project focuses on developing Cinnarizine microspheres using PLGA (Poly (lactic-co-glycolic acid)) and Chitosan to enhance the drug's delivery for treating vertigo and Ménière's disease [1]. Cinnarizine, a histamine analog with a short half-life and frequent dosing needs, suffers from fluctuating plasma levels and poor patient compliance in its conventional oral form. By encapsulating it in microspheres, this study aims to achieve controlled release, leveraging PLGA's biodegradable [2], tunable properties for sustained delivery and Chitosan's mucoadhesive, biocompatible nature to improve stability and retention. Through techniques like solvent evaporation or emulsification, the project will synthesize and characterize these microspheres, assessing their size, encapsulation efficiency, and release profile, to overcome current therapeutic limitations and advance efficient drug delivery systems [3].

Cinnarizine is an active histamine analog primarily used in the treatment of vertigo, tinnitus, and Meniere's disease—conditions related to vestibular disorders and inner ear dysfunction [4]. It acts as a partial agonist at histamine receptors (H1 and H3), primarily targeting H3 receptors in the inner ear, and plays a crucial role in improving blood circulation to the inner ear, thereby helping alleviate symptoms like dizziness and tinnitus. However,

Cinnarizine's clinical efficacy is hindered by its short half-life, rapid clearance, and limited oral bioavailability [5]. These pharmacokinetic limitations call for the development of novel drug delivery systems that can provide controlled and sustained release of Cinnarizine over an extended period [6].

The use of controlled drug delivery systems (DDS) has gained significant attention in pharmaceutical research as a strategy to overcome such challenges [7]. Among various drug delivery systems, microspheres, which are small, spherical particles capable of encapsulating drugs [8], have emerged as a promising option for controlled and sustained drug release [9]. Microspheres can be engineered to release the drug at a predetermined rate, minimizing the frequency of dosing while enhancing therapeutic efficacy and patient compliance [10]. Cinnarizine is used primarily to treat vestibular disorders, including vertigo, a common symptom associated with inner ear dysfunction [11].

Vertigo is often caused by conditions such as Meniere's disease, a disorder of the inner ear that causes severe dizziness, hearing loss, and a sensation of ringing in the ears (tinnitus) [12]. The drug works by improving blood flow to the inner ear, enhancing the function of the vestibular system and reducing symptoms related to dizziness and nausea [13].

Cinnarizine's mechanism of action is centered on its ability to act as a partial agonist at histamine receptors—specifically the H1 and H3 receptors [14]. It has been shown to increase blood flow in the cochlear region of the inner ear and to inhibit the release of certain neurotransmitters involved in vestibular dysfunction [15]. Despite its efficacy, the clinical use of Cinnarizine is limited due to several pharmacokinetic challenges [16].

2. Materials and Methods

2.1 Materials

a) Drug:

Cinnarizine Dihydrochloride – The active pharmaceutical ingredient (API) used in the formulation. Cinnarizine is usually available as a white, crystalline powder, which is soluble in water.

b) Polymers:

Polymers are key to controlling the release rate of the drug and ensuring the stability of the microspheres. Commonly used polymers in solvent evaporation techniques include:

Natural polymers:

Chitosan is used as natural polymer

Synthetic Polymers:

Poly(lactic-co-glycolic acid) (PLGA): A biodegradable polymer widely used in controlled drug delivery applications due to its ability to degrade into non-toxic metabolites (lactic acid and glycolic acid).

c) Solvents:

Organic Solvents – Used for dissolving the polymer and/or drug. Common solvents include:

Dichloromethane (DCM): Often used for its low boiling point and ability to dissolve hydrophobic polymers.

Chloroform: A widely used solvent that can dissolve both hydrophobic polymers and some drugs.

2.2 Methodology

a) Preparation of Polymer Solution:

Polymer Selection and Dissolution:

Select the polymer based on the desired drug release profile and prepare a polymer solution by dissolving a suitable amount of the polymer (e.g., PLGA or gelatin) in an organic solvent (e.g., dichloromethane or chloroform). The concentration of the polymer solution typically ranges from 1% to 10% (w/v), depending on the desired final microsphere characteristics.

Drug Loading:

Cinnarizine is dissolved or dispersed in the polymer solution. The concentration of the drug is typically adjusted based on the desired drug load (e.g., 10–50% w/w of the

polymer). The drug is either dissolved in the organic solvent along with the polymer or suspended if it is poorly soluble in the solvent.

b) Emulsion Formation:

Preparation of the Aqueous Phase:

The aqueous phase is prepared by dissolving stabilizers like polyvinyl alcohol (PVA) in water. The concentration of PVA is usually between 1% to 2% (w/v). The purpose of the aqueous phase is to prevent the coalescence of the organic phase (which contains the polymer and drug) during emulsification.

Emulsification Process:

The organic phase (containing the polymer and drug) is added dropwise to the aqueous phase under continuous stirring. This forms a primary emulsion (O/W: oil-in-water). High-speed homogenization or sonication may be applied to reduce the droplet size and ensure uniform emulsification. This step is crucial for achieving microspheres with uniform size and drug distribution.

The emulsion is typically prepared under cold conditions (e.g., using an ice bath) to prevent premature evaporation of the solvent.

c) Solvent Evaporation:

Evaporation of the Organic Solvent:

After emulsification, the solvent is evaporated to harden the microspheres. This is achieved by stirring the emulsion at room temperature or under reduced pressure (using a rotary evaporator). During this step, the organic solvent (e.g., dichloromethane or chloroform) evaporates, leaving behind solidified microspheres of the polymer and encapsulated drug.

Completion of Microsphere Formation:

As the solvent evaporates, the polymer solidifies, trapping the Cinnarizine inside the microsphere matrix. This results in the formation of spherical microparticles.

d) Isolation of Microspheres:

After complete solvent evaporation, the microspheres are separated from the aqueous phase by centrifugation or filtration. The collected microspheres are then washed several times with water to remove any residual surfactant or unencapsulated drug.

e) Drying of Microspheres:

The microspheres are typically freeze-dried or air-dried to remove any residual water content. Freeze-drying helps preserve the microsphere structure and drug loading.

3. Results

3.1 Entrapment efficiency

Table -1: Formulation and Encapsulation efficiency

Formulation code	PLGA: Chitosan	Drug Load (%w/w)	Encapsulation Efficiency (EE) (%)
R1L1	PLGA70%: Chitosan 30%	10%w/w	82
R1L2	PLGA70%: Chitosan 30%	20%w/w	79
R1L3	PLGA70%:Chitosan 30%	30%w/w	72
R2L1	PLGA50%:Chitosan 50%	10%w/w	90
R2L2	PLGA50%:Chitosan 50%	20%w/w	88
R2L3	PLGA50%:Chitosan 50%	30%w/w	80
R3L1	PLGA30%:Chitosan 70%	10%w/w	68
R3L2	PLGA30%:Chitosan 70%	20%w/w	65
R3L3	PLGA30%:Chitosan 70%	30%w/w	60

The entrapment efficiency (EE) of microspheres refers to the percentage of the total drug (or active ingredient) that is successfully encapsulated within the microspheres, compared to the total amount of drug that was initially added during the preparation process.

3.2 Dissolution of Cinnarizine Microspheres

Dissolution of Microspheres carried out in PBS 7.4 using USP type II apparatus for 8 hours

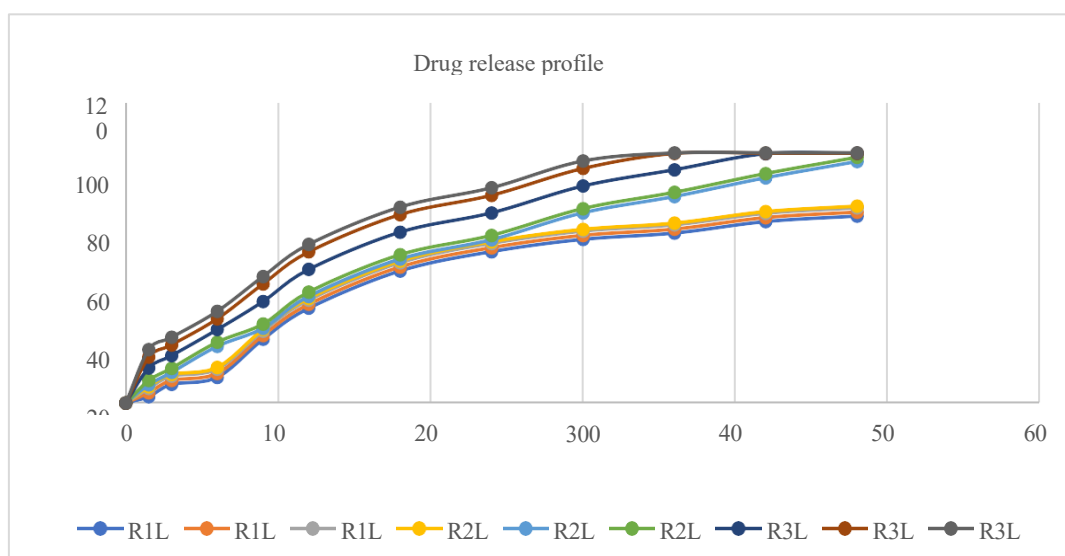


Fig -1: Dissolution data

4. Conclusion

Among the various formulations, R2L2 emerged as the optimum formulation, exhibiting favorable characteristics in terms of drug entrapment efficiency and controlled drug release. This formulation demonstrated an initial burst release, followed by a sustained release profile, making it a suitable candidate for extended drug delivery.

Further optimization in polymer ratios and process parameters may refine the formulation, enhancing reproducibility and clinical applicability. Future studies should focus on in vivo pharmacokinetic assessments and stability studies to validate the formulation's potential for therapeutic applications.

References

- [1]. Appasaheb PS, Manohar SD, Bhanudas SR, Anjaneri N. "A review on intranasal drug delivery system." J. Adv. Pharm. Edu. & Res. 2013, 3(4), 333-346.
- [2]. Alam MI, Beg S, Samad A, Baboota S, Kohli K, Ali J, Ahuja A, and Akbar M, "Strategy for Effective Brain Drug Delivery." Eur. J. Pharm. Sci. 2010, 40, 385–403.
- [3]. Ugwoke MI, Verbeke N, Kinget R. "The biopharmaceutical aspects of nasal mucoadhesive drug delivery." Journal of pharmacy and pharmacology. 2001,53(1),3-22.
- [4]. Arora P, Sharma S, Garg S. "Permeability issues in nasal drug delivery. Drug discovery today.2002,7(18),967-75.

- [5]. Singh AK, Singh A, Madhv NS. "Nasal cavity, a promising transmucosal platform for drug delivery and research approaches from nasal to brain targetting." *Journal of drug delivery and therapeutics*. 2012,2(3),22-23
- [6]. Chhajed S, Sangale S, Barhate SD. "Advantageous nasal drug delivery system: a review." *International Journal of Pharmaceutical Sciences and Research*. 2011,2(6),1322.
- [7]. Zaheer A, Swamy S. "Mucoadhesive polymers: Drug carriers for improved nasal drug delivery." *Indian Journal of Novel Drug Delivery*. 2012,4(1),2-16.
- [8]. Behl C,R., Pimplaskar N.K., Sileno A.P., Demeireles J., and Romeo VD. "Effect of physicochemical properties and other factors on nasal drug delivery." *Advanced drug delivery Reviews*. 1998,89-116.
- [9]. Illum, L. "Transport of drug from the nasal cavity to central nervous system." *Eur J Pharm Sci*. 2000,11, 1–18.
- [10]. Mygind N, Dahl R. "Anatomy, physiology and function of the nasal cavities in health and disease." *Advanced drug delivery reviews*. 1998,5,29,3-12.
- [11]. Evans MJ, Plopper CG. "The Role of Basal Cells in Adhesion of Columnar Epithelium to Airway Basement Membrane." *Am Rev Respir Dis*, 1988,138,481- 483.
- [12]. J.L. Carson, A.M. Collier, R.C. Boucher, "Ultrastructure of the epithelium in the human nose," *Allergic and Vasomotor Rhinitis. Pathophysiological Aspects*. 1987, 11–27
- [13]. Widdicombe J. "Microvascular anatomy of the nose." *Allergy*. 1997,52,7-11.
- [14]. Viswanathan H, Brownlee IA, Pearson JP, Carrie S. "MUC5B secretion is up-regulated in sinusitis compared with controls." *American journal of rhinology*. 2006,5,554-7.
- [15]. M. Kaliner, Z. Marom, C. Patow, J. Shelhamer, "Human respiratory mucus." *J. Allergy. Clin. Immunol*. 1984, 73 ,318–323.
- [16]. Laursen TM, Nordentoft M, Mortensen PB. "Excess early mortality in schizophrenia." *Annual review of clinical psychology*. 2014 10,425-48.