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Research Article

Formulation and Characterization of Intranasal Mucoadhesive Gel of Antiallergic Drug Loratadine for Improved Bioavailability

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Abstract

The present study aimed to formulate and characterize an intranasal mucoadhesive gel of loratadine to enhance its bioavailability. Loratadine, an antihistamine, is commonly used for the treatment of allergic conditions, but its low bioavailability due to extensive first-pass metabolism can limit its effectiveness. To address this issue, an in situ gel formulation was developed using Poloxamer 407 and Carbopol 934 as excipients. The gel's physicochemical properties, including pH, drug content, viscosity, gel strength, gelation temperature, and drug release profile, were evaluated. FT-IR analysis revealed no significant chemical interaction between the drug and excipients, confirming the stability of the formulation. The gel exhibited shear-thinning behavior and gelation temperatures suitable for nasal administration. In vitro drug release studies showed a sustained release profile, with higher Carbopol concentrations resulting in slower drug release. The mucoadhesion time increased with Carbopol 934 concentration, ensuring prolonged retention at the nasal site. Stability studies demonstrated that the formulations remained stable under standard storage conditions. The results suggest that the loratadine-loaded mucoadhesive gel has the potential to improve the bioavailability of loratadine through intranasal delivery, offering a promising alternative to conventional oral dosage forms.

Keywords: Loratadine, Mucoadhesive Gel, Poloxamer 407, Carbopol 934, In Situ Gel, Bioavailability, Drug Release, Nasal Delivery, Stability, FT-IR

INTRODUCTION

Loratadine is a widely used antihistamine drug primarily indicated for the treatment of allergic conditions such as allergic rhinitis and urticaria. It acts by selectively inhibiting the histamine H1 receptors, providing relief from allergy symptoms such as sneezing, itching, and nasal congestion. However, despite its therapeutic efficacy, loratadine has limitations related to its bioavailability and pharmacokinetics. It undergoes significant first-pass metabolism in the liver, leading to a relatively low oral bioavailability, typically around 40% [1]. This limitation calls for alternative drug delivery systems that could improve its bioavailability and provide a more effective therapeutic outcome.

Recent advancements in drug delivery systems have explored the potential of intranasal administration, which offers several advantages over conventional oral formulations. The nasal route is a direct pathway to the systemic circulation, bypassing the first-pass effect of the liver, thereby potentially improving the bioavailability of drugs [2]. Furthermore, the nasal mucosa possesses high permeability, allowing for the rapid absorption of drugs. Intranasal formulations, such as gels, offer the added benefit of controlled and sustained release of the active pharmaceutical ingredient (API), improving patient compliance and therapeutic effectiveness.

Mucoadhesive gels are particularly promising for intranasal drug delivery as they can adhere to the nasal mucosa, providing localized drug action and extended retention time. Mucoadhesive polymers, such as carbopol, sodium alginate, and polycarbophil, are commonly employed in the formulation of these gels due to their ability to form strong bonds with the mucosal lining, enhancing drug retention and absorption [3]. These gels can also be tailored to achieve the desired release profile, ensuring a sustained release of loratadine.

The formulation of an intranasal mucoadhesive gel containing loratadine is expected to overcome the limitations associated with oral administration, improve bioavailability, and provide faster onset of action for allergic conditions. In addition, intranasal delivery offers a non-invasive, patient-friendly alternative to injection-based therapies, further enhancing its appeal for both pediatric and adult patients [4].

This research focuses on the development, formulation, and characterization of an intranasal mucoadhesive gel containing loratadine, with the aim of improving its bioavailability and therapeutic efficacy. The study will

assess the formulation's physicochemical properties, including gel strength, drug release, mucoadhesion, and stability, to ensure its suitability for clinical use.

MATERIAL AND METHODS

Material

The materials used in the formulation of the intranasal mucoadhesive gel of loratadine included loratadine sourced from Yarrow Pharmaceuticals, Mumbai; Carbopol 934 from Oxford Fine Chemicals, Mumbai; Poloxamer 407 from Sigma Aldrich; and solvents such as ethanol, methanol, and acetone, all procured from Oxford Fine Chemicals, Mumbai. Sodium dihydrogen orthophosphate and disodium hydrogen phosphate, also from Oxford Fine Chemicals, were used as buffers for the gel preparation. Distilled water was prepared as required for the formulation process.

Methods

FTIR spectroscopic analysis

The Fourier transformed infrared spectroscopic analysis of the procured drug sample was performed and the major absorption bands were compared with that of the spectral database of the drug to ascertain its identity. FTIR of physical mixture of the drug and the used polymers was also performed to observe to any possible interaction between the drugs and excipients (Carbopol 934, poloxamer 407).

Determination of gelation temperature

Temperature at which the liquid (sol) phase converts to gel form is termed as gelation temperature. The sol–gel transition temperature of the prepared *in-situ* gel formulations was determined by visual inspection method [5]. Briefly, the solutions of poloxamer 407 in the concentrations (15–20 % w/v) were prepared by stirring on a magnetic stirrer in a transparent 10 ml glass bottle sealed with paraffin. The vial was heated at constant rate with an increment of 1°C and the temperature at which the magnetic bead stopped moving due to gelation was considered as gelation temperature. Gels which showed gelation temperature very close to nasal temperature (32-34°C) were selected for further evaluation. Effect of Carbopol 934 on phase transition temperature was evaluated by dispersing different concentration (0.1–0.5 % w/v) in optimized poloxamer 407 solutions.

Formulation of *in situ* nasal gel

Poloxamer 407 gel was prepared by dissolving the optimized poloxamer 407 concentration in cold (4°C) water. The hazy solution formed was kept in refrigerator (2–4°C) overnight for complete dissolution resulting in a clear solution. Carbopol 934 (0.1 to 0.4 % w/v) concentration was added slowly to the optimized poloxamer 407 solution [68] containing drug with continuous stirring at 4°C (Table 1). Formulated gels where then finally stored at 4°C for further evaluation.

Table 1: Composition of intranasal gel formulations

Formulation Code	Drug (% w/v)	Poloxamer 407 (%w/v)	Carbopol 934 (%w/v)
LNG1	0.5	18	0.1
LNG2	0.5	18	0.2
LNG3	0.5	18	0.3
LNG4	0.5	18	0.4
LNG5	0.5	18	0.5

Evaluation of the gel formulations [6]

Physico-chemical properties of *in-situ* gel

The formulated gels were evaluated for pH, clarity, drug content, viscosity and gel strength.

Determination of pH

The pH of each formulation was determined by pH meter. Initially, the pH meter was calibrated using standard buffer solutions of pH 4 and pH. 1 mL of the formulation was diluted with distilled water and the pH of the solution was recorded by dipping the electrode in the solution.

Clarity testing

The clarity was checked visually by viewing the formulation alternately against white and black background and was graded as turbid (+), clear (++) and very clear (+++).

Drug content

Drug content was determined spectrophometrically using UV at 357 nm. 1 mL of the formulation was dissolved in 10 mL PBS 7.2 and suitably diluted. The absorbance of the resulting dilution was recorded on UV spectrophotometer.

Viscosity Determination

Viscosity of *in situ* gel system was determined using Brook field viscometer DV-1. Temperature of 37±0.5ºC was maintained and the spindle was lowered perpendicularly into both *in situ* sol and gel formulations which were placed in a beaker. The viscosity of each formulation was determined by applying 100 rpm speed.

Rheological Studies

The measurement of viscosity of prepared *in situ* gel was done with Brookfield viscometer. The *in situ*

formulations were rotated for 2 minutes at different speeds (10-100 rpm) for selected spindle. At each speed the corresponding dial reading was noted. The viscosity of different *in situ* gel formulations was measured at different speeds at room temperature.

Gel Strength

Gel strength was determined by placing a standard weight of 35 g onto 50 g of thermoreversible gel (placed in 100 ml beaker) maintained at gelation temperature using controlled water bath. The time in seconds by the weight to penetrate 5 cm deep into the container was recorded as gel strength.

In-vitro drug release study

Drug release from gel was determined by using Franz diffusion cell. Artificial dialysis membranes were soaked in receptor medium for 2h prior to use. Phosphate buffer saline (12 ml) pH 6.4 was added into the receptor chamber maintained at 34 ± 1°C. Gel equivalent to 2.5 mg of drug was placed into donor compartment and the setup was kept on stirring. Aliquots of 1ml were withdrawn at predetermined time intervals from receptor compartment and replaced with fresh buffer till 12 h. The samples were diluted suitably and analyzed spectrophotometrically at 225 nm and the amount of drug released was determined using calibration curve.

Stability Study

Stability studies of the formulations were carried out at 40 ± 2°C, 75 ± 5% RH at an interval of one month for 3 consecutive months. The results were compared with respect to gelation temperature, pH, viscosity, drug content and drug release to indicate stability for optimized formulation [7].

In-vitro mucoadhesion wash-off test

Mucoadhesive property of microspheres was determined by *in-vitro* adhesion test. Eggshell membrane was used for this purpose. A 2x1 cm piece of eggshell membrane were taken and fixed on a glass slide (kept at an angle of 45°C). About 100 mg microspheres were spread on rinsed, tissue specimen and hung onto one of the groves of a USP tablet disintegrating test apparatus containing 6.8 pH phosphate buffer. The disintegrating test apparatus was started, the tissue specimen showed regular up and down movements in a beaker. The time required for detaching of microspheres from mucosal surface membrane was recorded by visual inspection [8].

RESULTS AND DISCUSSION

The findings from the physicochemical and rheological evaluations of the intranasal mucoadhesive gel formulations containing loratadine demonstrated promising results, particularly in terms of gelation properties, drug release, and mucoadhesion.

The FT-IR spectra of loratadine (Figure 1) revealed characteristic peaks at 3026.05 cm^{-1} (C-H stretching), 1720.13 cm^{-1} (C=O stretching), 1589.72 cm^{-1} (Aromatic C=C bending), and 1313.34 cm^{-1} (C-N stretching), confirming the presence of loratadine's key functional groups. The interaction of loratadine with excipients such as Poloxamer 407 and Carbopol 934 was assessed using FT-IR spectra (Figures 2 and 3). The absence of significant shifts in key peaks suggests that there were no major chemical interactions between the drug and excipients, which is beneficial for maintaining the drug's integrity.

Poloxamer 407, a thermoresponsive polymer, showed different gelation behaviors depending on its concentration. As seen in Table 3, the gelation temperature decreased with increasing concentration of Poloxamer 407, from no gelling up to 42°C at 15% concentration to gelling temperatures of 29-30°C at 20% concentration. This temperature range is ideal for intranasal delivery, ensuring that the gel remains in a liquid form during instillation and transitions to a gel upon contact with body temperature, providing sustained drug release.

The formulations exhibited a pH range of 5.8 to 6.2, which is within the acceptable range for nasal mucosal administration. Table 4 shows that the drug content for all formulations was above 90%, indicating the accurate incorporation of loratadine. The gel strength and viscosity increased with higher Carbopol 934 content, which contributes to the gel's mucoadhesive properties, ensuring better retention at the nasal site. The gelation time for these formulations decreased from LNG1 (12.1 sec) to LNG5 (4.1 sec), indicating that Carbopol 934 contributes to a quicker gelation time at physiological temperature.

The rheological analysis (Table 5) showed a non-Newtonian shear-thinning behavior for all the gel formulations, as viscosity decreased with increasing shear rate. This behavior is typical for mucoadhesive gels, as it allows the gel to flow easily during instillation and forms a thicker layer on the mucosa to provide prolonged contact time and controlled drug release.

The in vitro drug release data (Table 6) indicated that all formulations exhibited a controlled release of loratadine, with LNG1 showing the fastest release and LNG5 the slowest. This suggests that increasing Carbopol 934 concentration can retard the drug release, which is desirable for sustained drug delivery. The release profiles were in accordance with the typical expectations for mucoadhesive gels, with an initial burst release followed by a controlled release phase.

Mucoadhesion is critical for ensuring prolonged contact of the drug with the nasal mucosa. As seen in Table 7, the mucoadhesion time of the formulations increased with higher concentrations of Carbopol 934, ranging from 2.18 hours for LNG1 to 5.07 hours for LNG5. This suggests that Carbopol 934 enhances the gel's adhesive properties, promoting extended retention time at the nasal mucosal site.

Stability studies conducted under ICH guidelines (Q1A (R2)) demonstrated that the formulations remained stable after 1, 2, and 3 months, with no significant changes in key parameters like gelation temperature, pH, viscosity, drug content, and drug release. This

indicates that the formulations are stable under typical storage conditions and can be considered for clinical use.

Table 2: Major peaks occurring in the FT-IR spectra of loratadine

S. No.	Wave Number	Peak Occurs Due to...
1	3026.05	C-H stretching (alkyl)
2	1720.13	C=O stretching
3	1589.72	Aromatic C=C bending
4	1313.34	C-N stretching

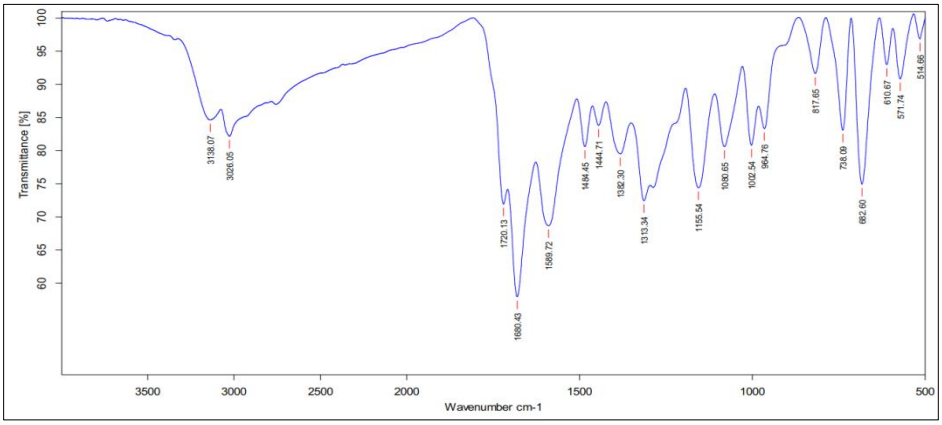

Figure 1: FT-IR spectra of loratadine

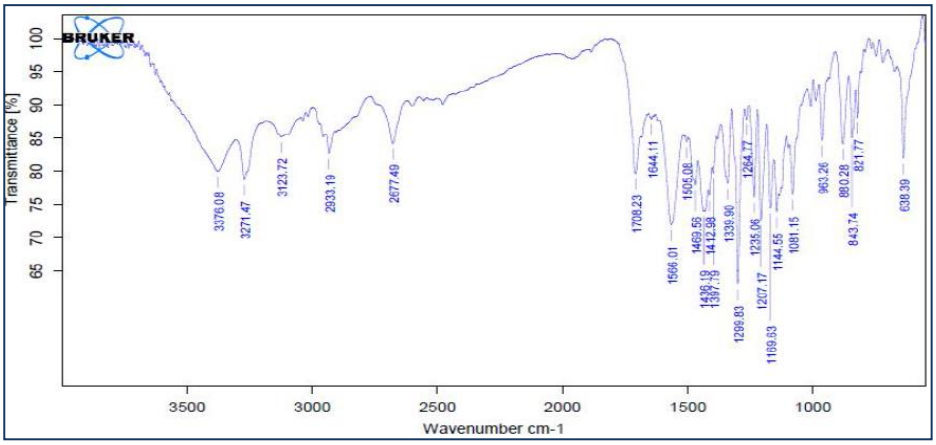

Figure 2: FT-IR spectra of loratadine + poloxamer 407

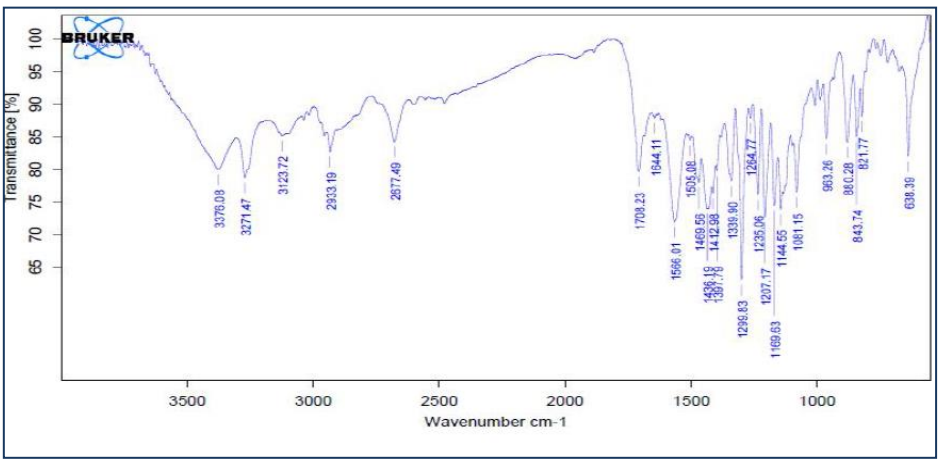

Figure 3: FT-IR spectra of loratadine + Carbopol 934

Table 3: Gelation temperature of Poloxamer 407

S. No.	Poloxomer 407 (%w/v)	Gelation Temperature (°C)
1	15	No gelling till 42
2	16	No gelling till 42
3	17	Viscous solution at 37
4	18	32-34
5	19	29-30
6	20	25-26

Table 4: Physicochemical properties of the *in situ* gel formulations

Formulation code	pH	Clarity	Drug content (%)	Viscosity (cps)		Gel Strength (g)	Gelling time (sec)
				Sol	Gel		
LNG1	5.8	+++	90.2	28	110	4.8	12.1
LNG2	6	++	93.9	35	122	5.5	10.1
LNG3	6	++	92.8	46	163	6.3	8.1
LNG4	6.1	+	93.6	57	180	7	6.1
LNG5	6.2	+	94.5	78	205	7.8	4.1

Table 5: Rheological behaviour of the gel formulations

Formulation code	Viscosity (cps)					
	10 rpm	20 rpm	40 rpm	60 rpm	80 rpm	100 rpm
LNG1	157	145	121	97	74	56
LNG2	162	150	129	101	90	72
LNG3	170	161	140	117	102	86
LNG4	181	173	149	134	110	98
LNG5	190	181	158	145	127	110

Table 6: *In vitro* drug release from the *in situ* gel formulations

Time (min)	LNG1	LNG2	LNG3	LNG4	LNG5
2	8.1	6.2	5.8	4.5	4.0
4	19.5	14.4	12.4	10.7	8.8
6	34.6	28.2	34.8	34.5	40.3
8	50.4	39.8	33.3	32.3	35.2
10	68.7	48.0	44.4	40.6	37.1
12	88.1	65.1	51.2	47.8	42.7
14	100.1	79.2	63.7	59.0	48.1
16		90.5	76.0	65.7	57.8
18		97.7	86.9	74.5	64.4
20			96.2	84.0	77.6

Table 7: Mucoadhesion of the gel formulations

Formulation Batch	Mucoadhesion time (h)
LNG1	2.18
LNG2	2.51
LNG3	4.15
LNG4	4.56
LNG5	5.07

CONCLUSION

The intranasal mucoadhesive gel formulations of loratadine developed in this study showed excellent physicochemical properties, controlled drug release, and desirable mucoadhesion characteristics. The formulations were stable over time and demonstrated effective drug release for prolonged nasal retention, making them a promising alternative for improving the bioavailability of loratadine. The use of Poloxamer 407 and Carbopol 934 has shown to be effective in enhancing the gel's properties, making it a suitable candidate for intranasal drug delivery.

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