AMERICAN JOURNAL OF PHARMTECH RESEARCH
Journal home page: http://www.ajptr.com/

Design and Characterization of A Loratadine-Loaded Ethosomal Gel For Transdermal Drug Delivery

Pooja PN*[1], Dr. V. Felix Joe[1]
1.Department of Pharmaceutics, Shree Devi College of Pharmacy, Kenjar, Mangaluru, Karnataka -574142, India.

ABSTRACT

This study examined loratadine-loaded ethosomal dispersions and the incorporation of the selected batch into a Carbopol-based gel for potential topical/transdermal use. Eight distinct formulations (F1–F8) were prepared and subsequently evaluated for vesicle size, drug entrapment and *in-vitro* release. Particle size ranged from 118.6 ± 2.41 nm for F1 to 236.8 ± 4.12 nm for F8; entrapment efficiency ranged from 72.64% to 87.35%. F8 showed the highest entrapment efficiency (87.35%) and drug release was 90.18% over seven hours. The selected F8 dispersion was mixed with Carbopol gel and tested for viscosity, spreadability, pH and drug content. Drug content was found to be 98.46%, while cumulative release reached 87.35% at seven hours. Of the kinetic models assessed, the Higuchi model had the highest coefficient of determination ($R^2 = 0.9997$). No visible irritation was recorded during the 14-day observation period. Stability study was carried out for four-weeks under specific storage conditions. Overall, the experimental findings identify F8 as the strongest candidate among the batches tested, based on entrapment, release and measured gel properties. These *in-vitro* findings justify further investigation but do not establish clinical effectiveness or confirm transdermal delivery in humans. Further studies, including appropriate skin-permeation testing and well-documented stability assessment, are needed.

Keywords: Loratadine, Ethosomes, *In-vitro* drug release and skin irritation studies.

*Corresponding Author Name: Pooja Podonolana
Received 26 September 2026, Accepted 06 October 2026

Please cite this article as: Pooja PN *et al*., Design and Characterization of A Loratadine-Loaded Ethosomal Gel For Transdermal Drug Delivery. American Journal of PharmTech Research 2026.

INTRODUCTION

Topical preparations are applied to the body's external surfaces and may be designed to treat a local condition or, in some cases, deliver an active ingredient across the skin. Gels are convenient semisolid vehicles, but the amount of drug release and product performance depend on the properties of the active substance and the formulation base.[1]

The stratum corneum forms the principal barrier to the passage of many compounds through skin. Consequently, a drug's physicochemical characteristics can limit its ability to permeate the skin and reach the intended site.[2]

Ethosomes are vesicular carriers made from phospholipids, ethanol and water. Ethanol can influence the flexibility of the vesicle membrane and interact with skin lipids; these effects may facilitate movement of an incorporated drug across the skin barrier.[3]

A gel containing ethosomes may combine the potential skin-penetration benefits of the vesicles with the ease of application associated with semisolid dosage forms. The gel vehicle also helps the product remain distributed over a selected area.[4]

Loratadine (LRTD) is a non-drowsy antihistaminic available as a tablet, mouth-dissolving tablet, and solution, prescribed for the treatment of allergies associated with itching and redness due to insect bites. However, conventional oral administration shows variable absorption. Hence, an alternative approach of delivering LRTD topically can be beneficial to overcome the difficulties and associated side effects of conventional dosage forms. Topical delivery allows the drug to be localized at the site of skin allergies, providing rapid relief and better patient compliance. While its low molecular weight and daily dose partially qualify LRTD as a candidate for dermal delivery, its high lipophilicity and very poor water solubility can hinder skin permeation. Therefore, permeability can be improved by incorporating LRTD into colloidal drug carrier systems; specifically, ethosomes can be planned for this purpose, as researchers have proven that they enhance transdermal penetration.[5]

MATERIALS AND METHOD

Materials

Loratadine was procured from Yarrow Chemicals, Mumbai, India. Soya lecithin was supplied by Oxford Lab Fine Chem LLP, Maharashtra, India. Cholesterol and Carbopol 934 were procured from Yarrow Chemicals. All other chemicals and reagents were of sufficiently high purity and quality for laboratory analysis and scientific experiments.

Pre-formulation studies

Preformulation tests were performed to describe the drug's physical and chemical properties and to inform selection of excipients and dosage-form design.

Identification of drug

To identify the drug, the physical form, colour and odour of the sample were visually inspected and compared against the available pharmacopoeial description.

Colour: A small amount of the sample was placed on butter paper and examined under adequate illumination.

Odour: Assessment of odour was carried out on small quantity of the sample.

Solubility studies

Solubility of the drug was investigated in water and standard organic solvents like acetone, chloroform, ethanol, methanol and ether.

Determination of melting point

Capillary method was used to determine the melting point of the drug. A small amount of sample was sealed in a capillary tube, placed in the melting-point apparatus and heated gradually. The temperature ranges from the start of melting until the sample had fully melted was recorded.

Determination of drug pH

The pH was determined by a digital pH meter using a freshly prepared 1% loratadine solution in ethanol.

FTIR studies

FTIR spectra of loratadine, selected excipients and their physical mixture were compared to look for notable changes in characteristic functional-group bands. Samples were prepared as moisture-free potassium bromide pellets and analyzed with an infrared spectrophotometer. The spectra were assessed for evidence of possible drug–excipient interactions.[6]

Analytical methods

Preparation of phosphate buffer pH 7.4:

To prepare 1 L of pH 7.4 phosphate buffer, 2.38 g disodium hydrogen phosphate, 0.19 g potassium dihydrogen phosphate and 8.0 g sodium chloride were dissolved in water, before adjusting the final volume to 1L and checking the pH.

Determination of λ_{max} of loratadine

Primary stock preparation: A Primary stock solution (1000 µg/mL) was prepared by dissolving 100 mg of loratadine in ethanol within a 100 ml volumetric flask, subsequently adjusting to volume with pH 7.4 phosphate buffer.

An intermediate stock solution (100 µg/mL) was generated by diluting a 10ml aliquot of the primary stock to 100 ml with the same buffer.

A final working stock solution (10 µg/mL) was obtained by further diluting 10 ml of the intermediate stock to 100 ml.

Analytical methods for estimation of loratadine

The prepared loratadine stock solution in 7.4 pH buffer was scanned across a wavelength range of 200 to 400 nm using a UV–visible spectrophotometer to determine the maximum absorbance wavelength.

Construction of calibration curve of loratadine

Serial standard solutions were prepared by transferring aliquots of 0.2, 0.4, 0.6, 0.8, 1.0 and 1.2 mL from the 10 µg/mL working stock solution into individual 10 ml volumetric flask and diluting to volume with pH 7.4 phosphate buffer.

The absorbance of each dilutions was measured at 245 nm against a phosphate buffer blank.

All measurements were performed in quintuplicate (n=5) and the resulting mean absorbance were used to construct the calibration curve.

Formulation of ethosomes

Loratadine loaded ethosomes were prepared via the hot method. Soya lecithin was dispersed in purified water and heated using a water bath at 40°C until a uniform colloidal dispersion was obtained. Ethanol and propylene glycol were combined and warmed independently to 40°C.

The organic phase was subsequently incorporated into the aqueous phase under controlled conditions to form the ethosomal system.

Eight distinct batches were formulated by systematically varying the concentration of phospholipid and ethanol, while the all other ingredients were maintained at a constant level. These formulations were subsequently evaluated for their specific physiochemical traits and utilized in further characterization studies.[7]

Table 1: Composition of different Loratadine ethosomal formulations

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Soya lecithin (mg)	0.1	0.1	0.1	0.2	0.2	0.2	0.3	0.3
Ethanol (ml)	5	10	15	5	10	15	5	10
Propylene glycol (ml)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Cholesterol (mg)	10	10	10	10	10	10	10	10
Drug (mg)	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Distilled water (ml)	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs

Characterization of loratadine ethosomes

Vesicle shape

Scanning Electron Microscopy (SEM) was employed to evaluate the vesicle shape surface morphology of the ethosomal vesicles. To prepare the sample, a single drop of the ethosomal formulation was placed onto a transparent glass stub and allowed to airdry. Subsequently, the specimen was coated with Polaron E5100 Sputter coater before being analyzed under the microscope.[8]

Particle size

The mean size of the developed ethosomes was evaluated using dynamic light scattering. Specifically, a Malvern zeta sizer was utilized to measure the precise vesicle dimension during the particle size analysis.

Zeta potential

Zeta potential indicates the electrokinetic potential near a particle's surface and provides information about electrostatic interactions within a dispersion. The result should be interpreted alongside particle size and storage findings rather than treated as a stand-alone proof of stability. Measurements were made at 25 °C using a Malvern Zetasizer (UK).[9]

Entrapment efficiency

To estimate entrapment efficiency, centrifugation method was used. Here, the centrifugal force separates the components according to their size and density. To evaluate entrapment efficiency 15 mL sample volume was subjected to centrifugation at 12,000 rpm for 1 hour.

Following this separation process, the concentration of the active compound remaining within the supernatant layer was quantified at 245 nm using UV spectrophotometric analysis.

The percentage entrapment efficiency was calculated according to the following mathematical relationship.

$$\%\text{Entrapment efficiency} = [\{Qt\text{-}Qs\}Qt]\times 100$$

Where, Q_t is the amount of drug added

Q_s is the amount of drug detected in the supernatant.[10]

***In-vitro* drug release studies**

The *in-vitro* release profile of loratadine from the prepared ethosomal suspension was evaluated using a Franz diffusion cell consisting of donor and receptor compartments. The receptor compartment was filled with 25 mL of phosphate buffer of pH 7.4 and equipped with a small magnetic stirring bead to maintain uniform mixing throughout the experiment, with the temperature of the receptor medium maintained at 37 °C to provide controlled experimental conditions. A cellophane membrane, previously immersed in phosphate buffer of pH 7.4, was positioned between the two compartments to act as a diffusion barrier. Approximately 1 g of the

loratadine-loaded ethosomal suspension was then applied to the membrane on the donor side. Samples were collected from the receptor medium at predetermined time intervals over a period of 7 hours. After each withdrawal, an equal volume of fresh phosphate buffer was added to maintain the receptor volume and provide sink conditions during drug release. Finally, the collected samples were diluted appropriately using phosphate buffer of 7.4 pH, and their absorbance was measured using a UV-visible spectrophotometer to determine the amount of loratadine released over time.[11]

Drug release kinetics

To analyze the data gathered from the drug release study, zero-order, first-order, Higuchi and Korsmeyer-Peppas kinetic models were applied.

Formulation and characterization of loratadine ethosomal gel

Formulation of the ethosomal gel incorporated with loratadine

To prepare the loratadine ethosomal gel base, 1 g of Carbopol 934 was dispersed in distilled water and left overnight to hydrate. Triethanolamine was added to neutralize the dispersion and produce a transparent gel. Subsequently, the ethosomal suspension was thoroughly blended into the 19% Carbopol 934 gel base until a homogeneous mixture was achieved.[12]

Evaluation of ethosomal gel incorporated with loratadine

Physical evaluation of ethosomal gel

The practical characteristics and visual appearance of the formulated Loratadine ethosomal gels – specifically ease of washing and conclusiveness were assessed.

Measurement of pH of ethosomal gel

To determine the pH 1 gram of the fabricated loratadine ethosomal gel was dispersed into 100 ml of distilled water.

The pH of the prepared loratadine ethosomal gel was determined by dispersing 1 g of the formulation in 100 mL of distilled water. The mixture was homogenized systematically to obtain a uniform dispersion. The electrode of a calibrated digital pH meter was then immersed in the prepared sample, and the pH reading was recorded after stabilization. The measurement was performed in triplicate to ensure consistency and reliability, and the mean pH value was calculated from the three readings.[13]

Viscosity

Viscosity of loratadine ethosomal gel was determined with a Brookfield DV-II+Pro viscometer (model D220) using spindle 64. Approximately 50 g of gel was transferred to a 50 mL beaker, and the spindle groove was immersed in the sample. Readings were taken at 5, 10, 50 and 100 rpm. Different rpm were set (5,10,50,100) and the dial reading was measured.[14]

Washability

To evaluate washability the gel was spread onto the skin and its ease of rinsing with water was assessed.[15]

Spreadability

Spreadability is a term used to denote how readily a gel spreads on the skin upon application on affected area. To assess spreadability the time required for two glass slides to separate under a specific load was recorded after placing the gel between them. The calculation used was S = M × L/T, where M is the weight attached to the upper slide, L is the slide length and T is the separation time. The less time taken for the two slides to separate, the better is the spreadability. Spreadability was calculated using the formula:

$$S = M \times L/T$$

Where,

M = weight tied to upper slide

L = length of glass slides

T = time taken to separate the slides.

For the measurement, 1 g of gel was placed between two glass slides marked in 5 mm squares and left for approximately five minutes. The spread area was measured in centimetres and were taken as comparative values for spreadability. A 125 g weight was attached to the upper slide, and the reported value was based on three measurements.[16]

Drug content

The drug content of the prepared loratadine ethosomal gel was determined using UV-visible spectrophotometry. Briefly, 100 mg of the gel was dissolved in 100 mL of phosphate-buffered saline (PBS, pH 7.4). A 1 mL aliquot of this solution was further diluted to 100 mL with PBS (pH 7.4). The absorbance was measured at 245 nm against an appropriate blank. Loratadine concentration was quantified using a pre-established standard calibration curve, and the total drug content was calculated after applying the dilution factor.

$$\text{Amount of drug} = (\text{concentration from the standard graph} \times \text{DF})/1000$$

Where,

DF = dilution factor[17]

***In-vitro* drug release studies**

The drug release profile of the formulated loratadine ethosomal gel was evaluated using a Franz diffusion cell system. The setup consisted of donor and receptor chambers separated by a cellophane membrane presoaked in phosphate buffer (pH 7.4). Approximately 1 g of the

ethosomal gel was placed on the membrane within the donor chamber, while the receptor chamber was filled with 25 mL of the same buffer, maintained at a controlled temperature, and subjected to continuous magnetic stirring.

Over a 7-hour period, aliquots were collected from the receptor medium at predetermined intervals, and an equal volume of fresh buffer was immediately added to maintain a constant volume and preserve sink conditions. These collected samples were appropriately diluted with phosphate buffer (pH 7.4) and analyzed for absorbance using a UV-visible spectrophotometer. Finally, the concentration of released loratadine was calculated using a standard calibration curve to determine the drug release characteristics of the gel.[18]

***In-vitro* drug release kinetics**

The experimental data were analyzed using four models: zero-order, first-order, Higuchi, and Korsmeyer–Peppas model. The suitability of each model was assessed by fitting the observed drug release data to its corresponding kinetic equation. To understand the drug release behaviour and identify the mechanism involved, the *in-vitro* drug release results obtained for the loratadine ethosomal gel were evaluated using mathematical kinetic models. For the Korsmeyer–Peppas model, a graph was constructed by plotting the logarithm of cumulative percentage drug release against the logarithm of time, and the slope of this plot was used to determine the release exponent, which helps in understanding the drug release mechanism.[19]

Skin irritation study

Healthy rats of either sex (150-200 g) were used in the skin irritation study. The animals have unrestricted access to water and are fed a regular diet. Before the study began, the dorsal hair of the rats was completely shaved to mark a 5 cm^2 zone on both sides, designating one flank as the control and the opposite as the treated test site. After applying the prepared ethosomal gel for fourteen days, the location was monitored for any sensitivity and reactions.

Stability studies

Stability study is an important aspect of pharmaceutical formulation development, as it determines whether the active ingredient and finished dosage form retain their required quality during the storage. Formulation deterioration may be recognized through physical changes, including alterations in colour, odour, or consistency. In some cases, chemical degradation may occur without noticeable physical changes and can only be identified through appropriate analytical testing. The data obtained from stability studies help assess the formulation's quality over time and provide preliminary information for estimating its shelf life and identifying the need for formulation modifications.

In the present investigation, stability testing of the optimized loratadine ethosomal gel was conducted according to modified ICH guidelines. The formulation was examined for physical appearance, percentage drug content, and *in-vitro* drug release. Samples were stored under two different conditions in a stability chamber and evaluated after four weeks of storage. The observations and results obtained for the selected evaluation parameters were recorded and presented in tabular form.[20]

RESULTS AND DISCUSSION

Pre-formulation studies

The drug Loratadine was observed as an amorphous, white-buff powder with a bitter taste and was odourless. These observed characteristics were generally comparable with the reported characteristics, except for a slight difference in colour. The melting point of loratadine was observed to be 135 °C, which was within the reported range of 134-135 °C. The solubility study showed that loratadine was soluble in acetone, ethanol, methanol and chloroform, while it was insoluble in water. The poor aqueous solubility of loratadine supports the need for a suitable delivery system capable of improving drug incorporation and facilitating its delivery through the skin. Ethosomes were therefore selected as a vesicular carrier because their composition containing phospholipid and ethanol is suitable for incorporating poorly water-soluble drugs.

Analytical studies

Determination of λ_{max}

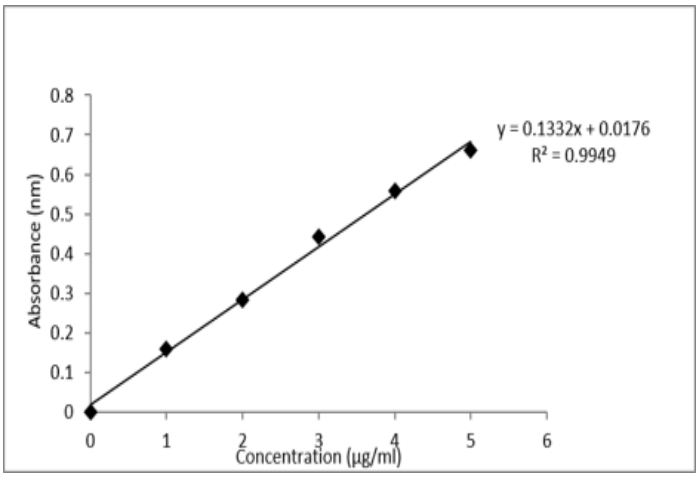


Figure 1: Standard curve of Loratadine

The drug showed maximum absorbance at 245nm. Therefore, 245nm was selected as the λ_{max} for the analytical studies and was thus used for the estimation of loratadine during subsequent investigations.

Calibration curve of loratadine

Scanning from 200 to 400 nm identified 245 nm as the absorption maximum for loratadine; this wavelength was used in the subsequent analyses.

Table 2: Calibration Data of Loratadine

Sl.no	Concentration (µg/ml)	Absorbance
1	0	0
2	1	0.158
3	2	0.284
4	3	0.483
5	4	0.557
6	5	0.651

A calibration analysis of loratadine was prepared using concentrations ranging from 0 to 5 µg/mL. As the absorbance increases drug concentration also increases.

The progressive increase in absorbance with concentration demonstrated the suitability of the selected UV spectrophotometric method for quantitative estimation of loratadine within the investigated concentration range. The calibration curve and its regression parameters were subsequently used for estimation of drug content and drug release during formulation and evaluation.

Drug excipient compatibility study

The FTIR spectrum of loratadine, soya lecithin, cholesterol and the physical mixture were evaluated side by side. Characteristic absorption bands in the individual components were compared with those in the mixture to assess potential incompatibility.

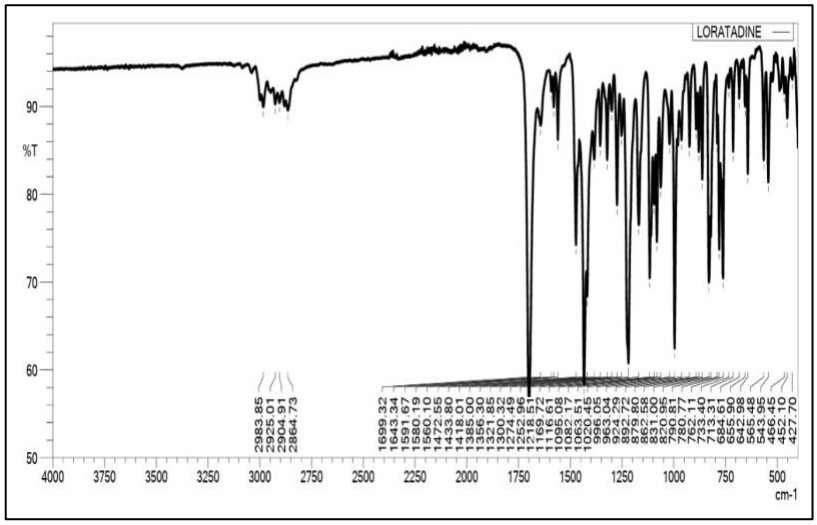


Figure 2: FTIR spectrum of Loratadine

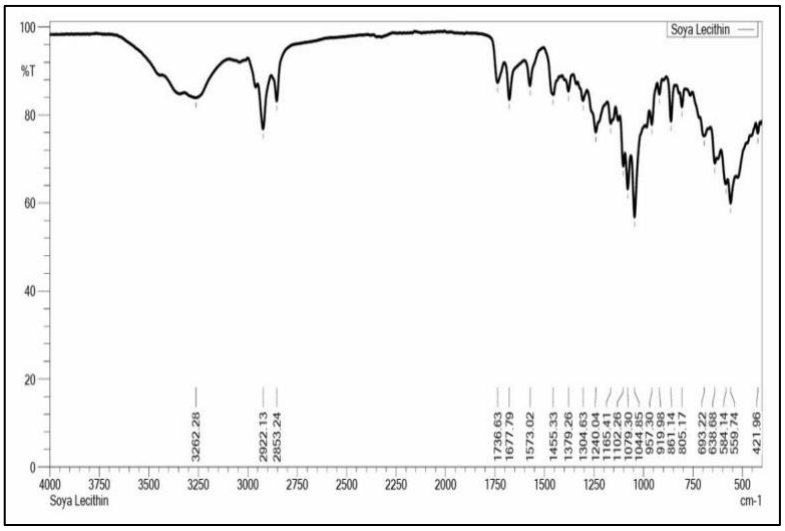


Figure 3: FTIR spectrum of Soya lecithin

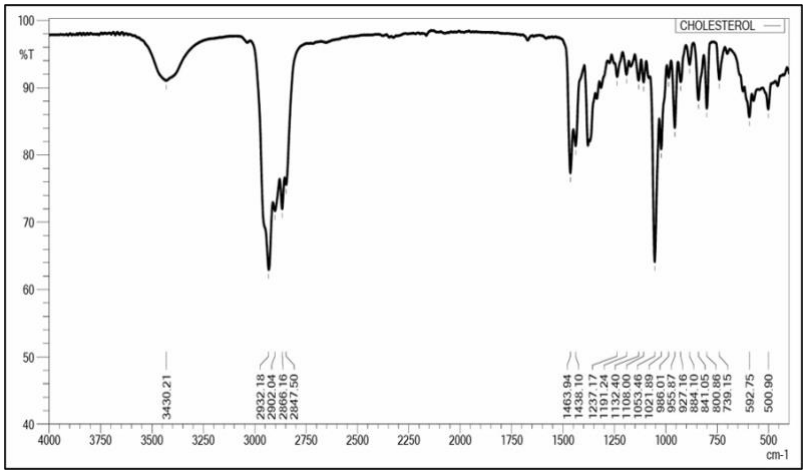


Figure 4: FTIR spectrum of Cholesterol

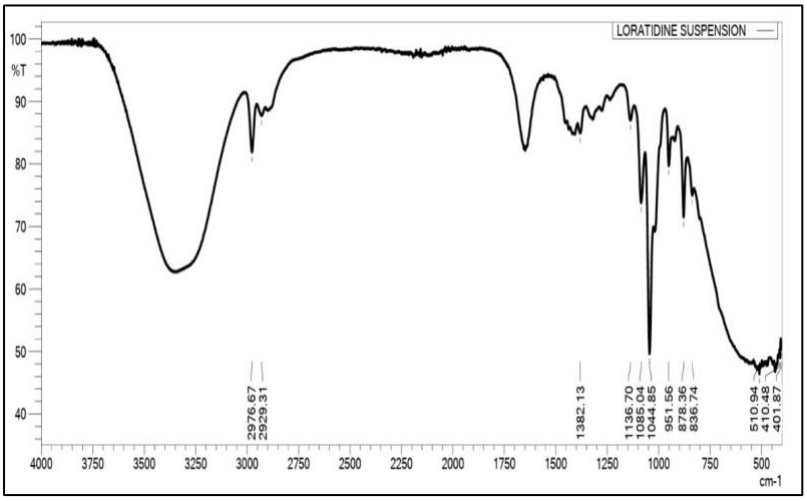


Figure 5: FTIR spectrum of Loratadine with physical mixture

The loratadine spectrum contained bands attributed to aliphatic C–H, carbonyl, C=C, C–N and ether groups. The soya lecithin spectrum showed bands assigned to hydroxyl, aliphatic C–H,

carbonyl, C=C, C–N, phosphate and ether groups; cholesterol showed its characteristic hydroxyl and other reported bands. The mixture retained broadly similar characteristic bands, with no major disappearance or pronounced shift reported. Under the conditions used, the FTIR findings therefore provided no clear evidence of a major interaction between loratadine and the selected excipients. These spectral observations support the use of soya lecithin and cholesterol in the preparation, although FTIR alone cannot be used for the formulation and evaluation of ethosomes.

Formulation of ethosomes

All eight formulations, F1–F8, of loratadine-loaded ethosomes were prepared and evaluated for important vesicular characteristics such as, vesicle morphology, zeta potential, particle size, zeta potential, entrapment efficiency and *in-vitro* drug release.

Characterization of ethosomes

Vesicle shape

SEM images showed distinct vesicle-like structures in the prepared dispersion, providing visual evidence consistent with vesicle formation.

Particle size

The measured mean particle size ranged from 118.6 ± 2.41 nm for F1 to 236.8 ± 4.12 nm for F8. The gradual increase in particle size among the formulations indicated that changes in formulation composition influenced the vesicle size. F8 formulation showed a Z-average particle size of 236.8 ± 4.12nm. The relatively small vesicle size provides a large surface area and is desirable for a vesicular drug delivery system for topical/transdermal application.

Table 3: Particle size analysis of Loratadine ethosomes

Formulation code	Particle size (nm)
F1	118.6 ± 2.41
F2	132.4 ± 3.16
F3	147.8 ± 2.73
F4	161.5 ± 3.24
F5	178.2 ± 2.89
F6	195.7 ± 3.52
F7	214.3 ± 3.67
F8	236.8 ± 4.12

*Where standard deviation, n = 3

Zeta potential

Zeta potential is an important physicochemical parameter used to evaluate the surface charge and colloidal stability of ethosomal vesicles. A higher absolute zeta potential generally produces stronger electrostatic repulsion between particles, thereby reducing the likelihood of vesicle aggregation. In the optimized formulation F8, the zeta potential was measured as −2.76 mV,

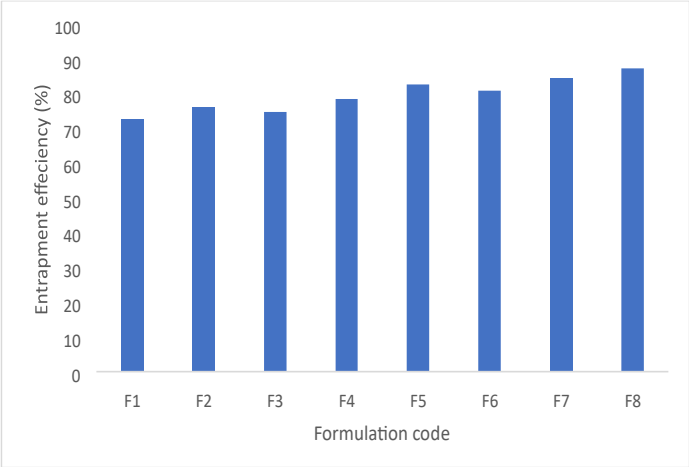
indicating a relatively low surface charge. Consequently, electrostatic repulsion may provide limited protection against particle aggregation. The physical stability of this formulation should therefore be confirmed through additional observations, such as particle size changes and stability testing during storage.

Entrapment efficiency

The entrapment efficiency was studied for the eight formulations in order to find out the best formulation for drug entrapment. The formulation F8 showed the maximum entrapment efficiency.

Table 4: Entrapment efficiency of loratadine ethosomes

Serial no	Formulation code	Entrapment efficiency (%)
1	F1	72.64
2	F2	76.28
3	F3	74.85
4	F4	78.46
5	F5	82.73
6	F6	80.91
7	F7	84.68
8	F8	87.35



*Where standard deviation, n = 3

Figure 6: % Drug entrapment efficacy of Loratadine ethosomal formulation

The entrapment efficiency of the eight formulations ranged from 72.64% to 87.35%. F1 showed the lowest value of 72.64%, whereas F8 exhibited the highest value of 87.35%.

The higher drug entrapment observed in F8 indicates that its formulation composition was more favourable for incorporating loratadine into the ethosomal vesicles. The relatively high entrapment efficiency is advantageous because it allows a greater proportion of the drug to be associated with the vesicular carrier.

Based on the highest entrapment efficiency, F8 was selected as the best ethosomal formulation for further studies.

***In-Vitro* drug release profile of loratadine ethosomes:**

Over the seven-hour release test, cumulative drug release had increased with time for each ethosomal batch. At seven hours, cumulative release ranged from 77.42% for F4 to 90.18% for F8. The F8 batch showed the highest reported release at the final sampling point. The combination of the highest entrapment efficiency and the greatest seven-hour release supported the choice of F8 for further formulation work. Release increased progressively during the test period. The data showed the drug release over the measured interval but do not by themselves establish the mechanism or clinical duration of action.

Table 5: *In-Vitro* Cumulative % drug release of ethosomes containing Loratadine

Time (min)	Cumulative % drug release							
	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	18.42	20.16	23.85	17.64	21.73	23.92	19.86	25.48
2	31.68	34.52	39.76	30.84	36.91	39.64	33.27	42.35
3	43.75	47.28	53.84	42.16	49.82	53.26	46.18	56.73
4	54.82	58.94	65.47	53.21	61.85	64.73	57.26	68.64
5	64.37	68.52	74.86	62.78	71.63	74.18	67.41	78.25
6	72.46	76.83	82.57	71.35	80.24	82.94	75.68	85.62
7	78.35	82.14	87.63	77.42	85.72	87.95	81.43	90.18

Formulation and characterization of loratadine ethosomal gel

Formulation of ethosomal gel

The ethosomal dispersions were incorporated into a gel base to obtain semisolid formulations. The formulated gels were then evaluated for pH, viscosity, spreadability and drug content.

pH

The pH values of the formulations ranged from 5.42 to 5.63. The values were within a mildly acidic range and showed only small variation among the formulations. This kind of pH values are suitable for transdermal/topical application and indicate that the formulations are unlikely to cause significant irritation due to extreme pH under the conditions of the study. F8 showed a pH of 5.63, indicating satisfactory pH characteristics for topical application.

Viscosity

Viscosity values extended from 5264 to 5896 cps. F8 had the highest recorded viscosity, 5896 cps, indicating a higher measured consistency under the test conditions.

Spreadability

The spreadability values ranged from 10.42 to 12.54 g/cm². F8 showed the highest spreadability value of 12.54 g/cm². Good spreadability is desirable for topical formulations because it facilitates uniform application over the skin surface. The combination of suitable viscosity and comparatively

higher spreadability indicated satisfactory physical characteristics of the F8 ethosomal gel.

Drug content

The drug content measured ranged from 92.18% to 98.46%. F8 showed the highest value, 98.46%. Considering the measured pH, viscosity, spreadability and drug content together, F8 was selected as the preferred gel batch in this study. The ethosomal formulations were incorporated into a gel to obtain a suitable topical/transdermal dosage form. The prepared gels were evaluated for pH, viscosity, spreadability and drug content.

Table 6. Characterization of ethosomal gel containing Loratadine

Formulation code	Measurement of pH	Viscosity (cps)	Spreadability (g/cm²)	% Drug content
F1	5.42	5794	10.42	92.18
F2	5.48	5324	10.64	93.64
F3	5.53	5535	10.86	94.27
F4	5.46	5677	11.24	95.13
F5	5.51	5301	11.68	96.42
F6	5.57	5264	11.82	97.18
F7	5.59	5400	12.16	97.83
F8	5.63	5896	12.54	98.46

***In-vitro* drug release from ethosomal gel**

The drug release behaviour of the formulated ethosomal gels was investigated using an *in-vitro* study conducted over 7 hours. A steady rise in cumulative drug release was observed across all formulations as the study progressed. After 7 hours, F1 exhibited the lowest drug release of 76.42%, whereas the best formulation F8 released 87.35% of the incorporated drug during the same period. The relatively slower release from the gel compared with the corresponding ethosomal suspension may be associated with the gel matrix, which creates an additional barrier to drug diffusion. However, F8 demonstrated considerable drug release throughout the study period, indicating its potential to provide sustained drug delivery.

Table 7. *In-Vitro* Cumulative drug release of ethosomal gel containing Loratadine

Time (hour)	Cumulative % drug release							
	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	15.86	18.24	20.73	16.42	19.68	22.54	18.31	21.46
2	28.74	32.16	36.82	29.53	34.75	39.42	31.68	36.94
3	40.86	44.73	50.64	41.28	48.62	54.18	45.27	51.73
4	51.92	56.48	62.87	52.74	60.35	66.42	57.16	63.85
5	61.47	66.35	72.84	62.18	70.24	76.43	66.91	73.26
6	69.85	74.62	80.76	70.48	78.16	83.74	75.21	81.56
7	76.42	81.37	86.58	77.16	84.73	89.46	82.18	87.35

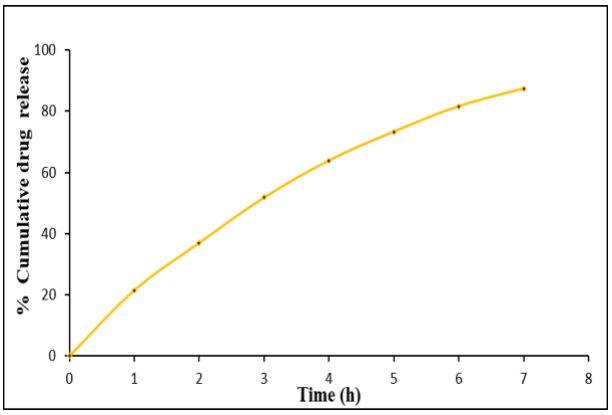


Figure 7: % cumulative drug release of ethosomal gel containing Loratadine

***In-Vitro* drug release kinetics of loratadine ethosomal gel**

The kinetic release of the best formulation were evaluated using zero-order, first-order, Higuchi and Korsmeyer–Peppas models.

The coefficient of determination (R^2) values were 0.9077 for zero-order, 0.9924 for first-order, 0.9997 for the Higuchi model and 0.9995 for the Korsmeyer–Peppas model.

Among the models investigated, the Higuchi model showed the highest coefficient of determination ($R^2 = 0.9997$), followed closely by the Korsmeyer–Peppas model ($R^2 = 0.9995$). The higher R^2 value for the Higuchi model indicates that the kinetic drug release of Loratadine ethosomal gel was best described by the Higuchi diffusion model under the conditions of the study.

Table 8: Drug Release Kinetics of F8 formulation

Time (hour)	% CDR	VT	Log T	Log % release	% CDR retained	Log % drug retained
0	0	0	0	0	100	2
1	21.46	1.000	0.000	1.500	68.35	1.835
2	36.94	1.414	0.301	1.6565	54.66	1.738
3	51.73	1.732	0.447	1.7372	45.4	1.657
4	63.85	2.000	0.602	1.7948	37.66	1.576
5	73.26	2.236	0.699	1.8465	29.77	1.474
6	81.56	2.449	0.778	1.8871	22.89	1.360
7	87.35	2.646	0.845	1.9164	17.51	1.243

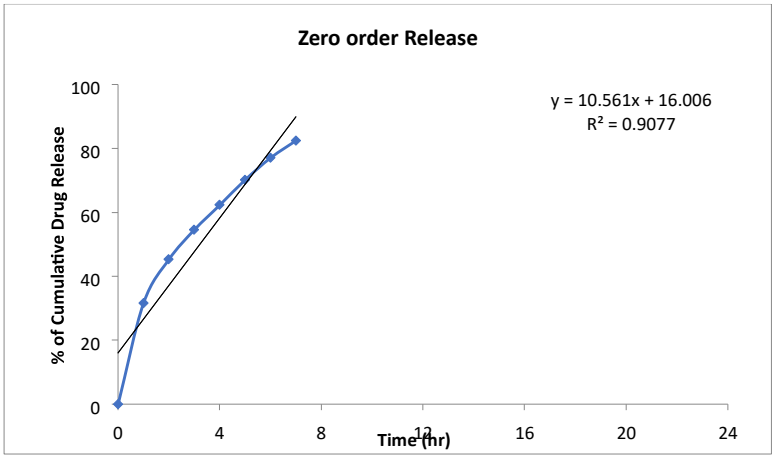


Figure 8: Zero Order Release Kinetics of F8 formulation

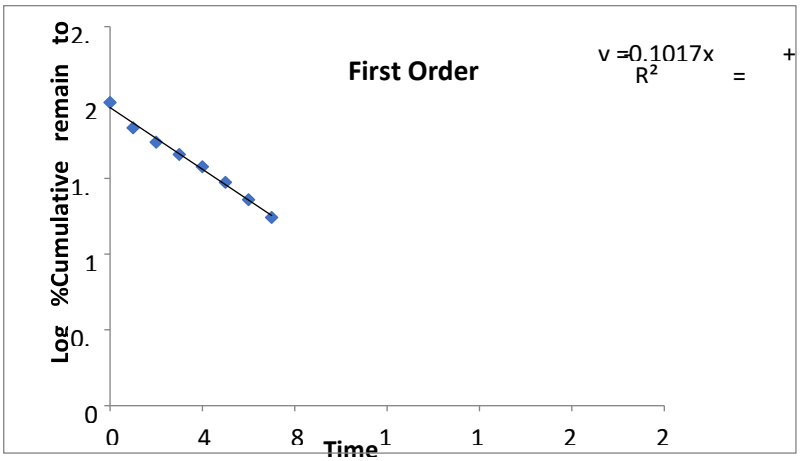


Figure 9: First Order Release Kinetics of F8 formulation

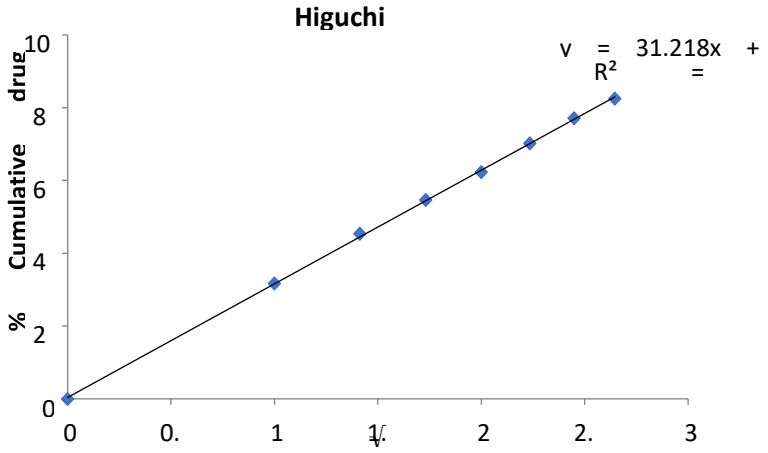


Figure 10: Higuchi's Model of F8 formulation

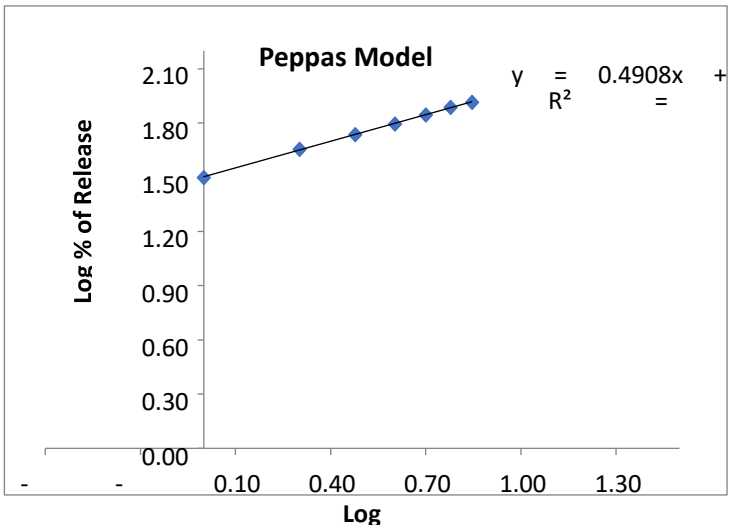


Figure 11: Korsmeyer-Peppas Model of F8 formulation

Table 9: Coefficient of Determination

Kinetics model	Coefficient of determination
Zero order	0.9077
First order	0.9924
Higuchi	0.9997
Peppas	0.9995

Skin irritation study

Table 10: Skin irritation test of ethosomal gel

Time period	Control panel	Test (F8)
Before application	0	0
1 hr	0	0
2 hr	0	0
48 hr	0	0
7 days	0	0
14 days	0	0

0 – No erythema, 1 – Slightly erythema, 2 – Patchy erythema, 3 – Severe erythema

At the control and F8 test sites, the recorded irritation score was zero before application and at each listed observation time: 1 hour, 2 hours, 48 hours, 7 days and 14 days. No visible irritation was recorded during the reported observation period. No visible irritation was observed in this test under the reported conditions. This finding is limited to the study design and does not establish safety for human use.

Stability studies of ethosomal gel containing loratadine

Table 11: Stability studies of ethosomal gel containing Loratadine

Formulation code	Parameters evaluated after 4 weeks	Storage temperature	
		25 °C+2 °C, 60%RH	**40 °C+2 °C, 60%RH**
F8	Appearance	Pale yellow, smooth gel	Pale yellow, smooth gel
	pH	6.0	6.2
	% Drug content	95.92	92.50
	% Drug release	85.12	82.45

The best ethosomal gel was subjected to stability testing for four weeks at 25 ± 2 °C/60% RH and 40 ± 2 °C/60% RH. The formulation maintained a pale-yellow, smooth-gel appearance under both storage conditions. The pH was 6.0 at 25 ± 2 °C and 6.2 at 40 ± 2 °C, showing only a small change during storage. The drug content was 95.92% at 25 ± 2 °C and 92.50% at 40 ± 2 °C. Similarly, the cumulative drug release was 85.12% and 82.45% at 25 ± 2 °C and 40 ± 2 °C, respectively. The comparatively higher temperature resulted in a small reduction in drug content and drug release. However, the formulated ethosomal gel retained its physical appearance and showed satisfactory drug content and release after four weeks. These findings indicate that F8 ethosomal gel possessed reasonable short-term stability under the investigated storage conditions.

CONCLUSION

Loratadine-loaded ethosomes were prepared and assessed as a possible vehicle for topical/transdermal delivery. Preformulation testing documented the drug's physical properties, UV spectrophotometry supported quantitative analysis, and FTIR spectra showed no major reported changes in characteristic bands after mixing with the selected excipients. SEM images showed vesicle-like structures. Among the eight batches, F8 had the highest entrapment efficiency (87.35%) and released 90.18% of the drug from the ethosomal dispersion over seven hours.

After combining the ethosomal formulation into carbopol gel, F8 showed a pH of 5.63, viscosity of 5896 cps and drug content of 98.46%. Cumulative release from the gel reached 87.35% at seven hours. The Higuchi model gave the highest R^2 value (0.9997) among the models compared. No visible irritation was recorded during the 14-day test.

Based on the measurements reported, F8 was the most promising batch among those evaluated.

Overall, the findings indicate that loratadine-loaded ethosomal gel possesses promising formulation characteristics, good drug entrapment, sustained *in-vitro* drug release, and acceptable skin tolerability under the experimental conditions. Therefore, ethosomal gel may be considered a potential carrier system for the transdermal delivery of loratadine. However, further *ex-vivo* skin

permeation studies, extended stability testing, and comparative investigations are required to establish its effectiveness and suitability for practical transdermal drug delivery.

ACKNOWLEDGEMENT

The author expresses sincere gratitude to Dr. V. Felix Joe, M.Pharm., Ph.D., Professor and Head, Department of Pharmaceutics, Shree Devi College of Pharmacy, Mangaluru, for his valuable guidance, constructive suggestions, and continuous encouragement throughout the research work. The author is also grateful to Dr. Jagadish V. Kamath, M.Pharm., Ph.D., Shree Devi College of Pharmacy, Mangaluru, for providing the necessary facilities to carry out this research. Special thanks are extended to Mrs. Smitha Shetty for her motivation, encouragement, and timely support. The author also acknowledges the support and cooperation of the faculty members, classmates, and friends of Shree Devi College of Pharmacy, Mangaluru. Finally, the author expresses heartfelt gratitude to her parents and family members for their unconditional love, prayers, and constant encouragement throughout her academic journey.

REFERENCE

1. Helal DA, El-Rehman DA, Abdel-Halim SA, El-Nabarawi MA. Formulation and evaluation of fluconazole topical gel. Int J Pharm Pharm Sci. 2012;4(5):176-83.
2. Barry BW. Novel mechanisms and devices to enable successful transdermal drug delivery. European journal of pharmaceutical sciences. 2001 Sep 1;14(2):101-14.
3. Touitou E, Dayan N, Bergelson L, Godin B, Eliaz M. Ethosomes-novel vesicular carriers for enhanced delivery: characterization and skin penetration properties. Journal of controlled release. 2000 Apr 3;65(3):403-18.
4. Jain S, Umamaheshwari RB, Bhadra D, Jain NK. Ethosomes: a novel vesicular carrier for enhanced transdermal delivery of an anti-HIV agent. Indian journal of pharmaceutical sciences. 2004;66(1):72-81.
5. Bhattacharyya S, Mohan U. Formulation and *In Vitro* Evaluation of Niosomal Gel of Loratadine: A Novel Topical Agent for Allergic Skin. Indian J Pharm Sci. 2023 Mar 1;85(2):325-37.
6. Fu X, Shi Y, Wang H, Zhao X, Sun Q, Huang Y, Qi T, Lin G. Ethosomal gel for improving transdermal delivery of thymosin B-4. Int J Nanomedicine. 2019:9275-84.
7. Fathima SA, Begum S. Fatima SS. Transdermal drug delivery system. Int J Pharm Clin Res. 2017;9(1):35-43.
8. Cevc G. Lipid vesicles and other colloids as drug carriers on the skin. Adv Drug Deliv Rev. 2014;56(5):675-711.

9. Indora N. Kaushik D. Design, development and evaluation of ethosomal gel of fluconazole for topical fungal infection. Int J Eng Sci Invent Res Dev. 2015;1(8):280-306.
10. Sathya SP, Parthiban S, Senthilkumar SK. Formulation and evaluation of captopril ethosomes as vesicular carrier. Int J Res Pharm Nano Sci. 2013;2(4):505-13.
11. Lamsal R, Geethalakshmi A, Gubbala S. Formulation and evaluation of gliclazide ethosomes as a novel drug carrier. Int J Pharm Sci Res. 2015;6(5):2072.
12. Madhavi BB, Vennela KS, Masana P, Madipoju B. Enhanced transdermal drug penetration of curcumin via ethosomes. Malays J Pharm Sci. 2013;11(1):49.
13. Indora N. Kaushik D. Design, development and evaluation of ethosomal gel of fluconazole for topical fungal infection. Int J Eng Sci Invent Res Dev. 2015;1(8):280-306.
14. Srivastava N, Singh K, Amrit K. Formulation and evaluation of seabuckthorn leaf extract loaded ethosomal gel. Asian J Pharm Clin Res. 2015;8(5):316-20.
15. Indira S, Priyanka R, Prathima S. Formulation and evaluation of ethosomal topical gels of Etoricoxib. Int J Pharm Res Sch. 2015;4(1):93-103.
16. Shukla KV, Sharma A, Yadav M. Formulation development and evaluation of ethosomal gel of acyclovir for the treatment of herpes zoster. J Drug Deliv Ther. 2019;9(4-A):664-8.
17. Thomas MA. Formulation and evaluation of ethosomal gel of tazarotene for topical delivery. Asian J Pharm. 2019;13(01).
18. Patil HN, Hardikar SR, Bhosale AV. Formulation development & evaluation of proniosomal gel of carvedilol. Int J Pharm Pharm Sci. 2012;4(1):191-7.
19. Fu X, Shi Y, Wang H, Zhao X, Sun Q, Huang Y, Qi T, Lin G. Ethosomal gel for improving transdermal delivery of thymosin B-4. Int J Nanomedicine. 2019:9275-84.
20. lizhar SA, Syed IA, Satar R. Ansari SA. In vitro assessment of pharmaceutical potential of ethosomes entrapped with terbinafine hydrochloride. J Adv Res. 2016;7(3):453-61.

