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Formulation and Evalution of Microemulsion based Loratadine Gel

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KEYWORDS

Loratadine, microemulgel, topical drug delivery, urticaria, and allergic rhinitis

ABSTRACT:

Introduction: A second-generation H1-antihistamine is loratadine. that is frequently used to treat urticaria and Rhinitis caused by allergies. However, contrary to, topical delivery is being investigated because of its low oral pH and first-pass metabolism bioavailability (~30%). The objective of this study is to create a loratadine-loaded microemulgel that will improve skin permeability and offer long-lasting medication release for efficient topical allergy treatment.

Objectives: This study's goal was to create and assess a loratadine-loaded microemulgel that would improve topical delivery for the treatment of allergic conditions by enhancing drug permeation, yielding prolonged release, and increasing bioavailability.

Methods: According to solubility studies, the best ingredients are propylene glycol, Tween 20, and ethyl oleate. Using pseudoternary phase diagrams, the optimal microemulsion regions were created. tests of thermodynamic stability, involving Centrifugation, heating-cooling cycles, and freeze-thaw cycles were all carried out. on a selection of formulations. The Carbopol 934 gel at 1% w/v was mixed with the optimised microemulsion. The pH, viscosity, drug content, spreadability, in vitro permeation (utilising a Franz diffusion cell and Strat-M® membrane), and drug release kinetics of the microemulgel were assessed.

Results: F2 had the best qualities of all the formulations a high drug content (97.26 ± 0.14%), good spreadability (6.5 ± 1.39 cm), and a pH that was skin-compatible (5.92 ± 0.28). A sustained drug release of 82.81% over a 24-hour period was found in vitro permeation studies. This was much higher than the control gel's (35.09%) and closely matched the microemulsion's 91.71% release. Drug release was consistent with the Korsmeyer–Peppas model (R2 = 0.992), which suggests a Transport mechanism for Super Case-II that includes polymer Relaxation and edoema in addition to diffusion. The microemulgel's chemical and physical stability over a month was validated by stability tests carried out in an ICH setting.

Conclusions: The loratadine-loaded microemulgel showed sustained drug release, superior physicochemical stability, and improved skin penetration. It offers a promising non-invasive substitute for the topical management of allergic skin diseases like allergic rhinitis and urticaria.

1. Introduction

Loratadine is an antagonist of the H-1 receptors of the second generation, has a quick, long-lasting effect without causing drawsiness and is utilised to treat allergic rhinitis and urticaria[1] The primary purpose of loratadine, a second-generation antihistamine, is to treat allergies.

Here's how it works. Loratadine inhibits the effects of histamine, a substance released during allergic reactions, by specifically blocking peripheral H_1 histamine receptors. H+ Receptors and Histamine attaches itself to H_1 receptors in the respiratory system, smooth muscles, and blood vessels. The symptoms of this binding include hives, runny nose, watery eyes, itching, and sneezing.

Journal of Chemical Health Risks
www.jchr.org
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Loratadine Action. Peripheral H+ receptors are competitively antagonistic to loratadine. By preventing histamine from binding, it lessens allergy symptoms [2]

It produces less sedation than first-generation antihistamines because it is lipophilic but does not easily pass across the blood-brain barrier.[3]Strong and long-acting, loratadine has little affection for central nervous system H1-receptors and a high selectivity. for peripheral histamine H1-receptors.Loratadine is an antiallergic medication that belongs to the BCS class 2 and has a 30% oral bioavailability.Topical medication Delivery is among the most promising at the moment. drug application methods. Takes away adverse effects like nausea and vomiting.Loratadine works by selectively inhibiting peripheral H1 receptors. Loratadine successfully stops histamine from binding and having its effects by blocking these receptors.[4,5]
External along with internal topicals are the two main categories of Products for topical drug administration. Where as Internal topicals are used. orally to mucus membranes on the tissues of the rectal cavity for local activity,, The outside Topicals are sprayed, spread, or applied in other ways. distributed throughout the tissue in order to cover the afflicted region. Preventing first-pass metabolism is among the primary benefits of topical medication delivery.[6]
Microemulgel is a formulation created by combining microemulsion and gel. The benefits of both emulgel and microemulsion were present in this formulation system. The ability to incorporate both Adding hydrophilic and hydrophobic medications to these systems is the system's primary benefit. These systems give the drug absorption a lot of surface area. By enhancing the drugs' permeability, the oil component raises bioavailability. When a microemulsion is integrated into a gel system, its stability is enhanced. As for microemulsions, microemulgel is easily washable and has a certain elegance.[7] Despite having the primary drawback of low viscosity characteristics, which make microemulsion unsuitable for use in dermatology, they are highly helpful in delivery of drugs topically due to their Good thermodynamic stability and minimal skin irritation, and simplicity of production. When gel and microemulsion are combined to create a microemulgel, the benefits of both formulation kinds are combined. The final formulation has several advantageous qualities, including being emollient, greaseless, thixotropic, spreadable, and easily removable, having a long shelf life, being clear, having a specific level of style, and being Washable with ease when needed. Furthermore, adding ME to gel lengthens its stability and retention period.[8]

2. Materials and methods

1) Materials

Dham Tec Pharma and Consultant in Navi Mumbai was the loratadine supplier. The ethyl oleate and propylene glycol were provided by Loba Chemie PVT. LTD. Clairofilt India is where we bought Tween 20 Every chemical and reagent used was of analytical quality. and underwent further purification.

2.1) oil, surfactant, and cosurfactant screening

For loratadine studies on solubility, a variety of microemulsion components were chosen, including oils (cinnamon oil, castor oil, sesame oil, orange oil, clove oil, lemongrass oil, and ethyl oleate), co-surfactants (Tween 20, Tween 40, and Tween 80) and surfactants. (propylene glycol, PEG 400, PEG 200, and ethanol.Excessive amounts of Cosurfactants, oils, and surfactants were added to the medication.After 48 hours of constant stirring in an orbital shaker, The mixtures were centrifuged for fifteen minutes at 3000 rpm.. It was the supernatant of then collected, diluted, and passed via a filter membrane of 0.45 µm before being looked at at 251 nm with a Visible UV spectrophotometer.[9]

2.2] Creating a pseudoternary phase diagram

To find the range of component concentrations with respect to the current various microemulsions, Diagrams of pseudo-ternary phases were produced. The weight ratios of surfactant to co-surfactant varied from 1:1 to 3:1 for each pseudo-ternary phase diagram. The greasy concoction comprising Co-surfactant, surfactant and oil were made using the oil to Smix weight ratio at 1:9, 1:8, 1:7, 1:6, 1:5, 1:4, 1:3, 1:2, 1:1 9:1, 8:1, 7:1, 6:1, 5:1, 4:1, 3:1, and 2:1, accordingly. There was water. gradually incorporated into each greasy combination using a suitable magnetic stirrer until it became clear. After The pseudo-ternary's phase diagrams showed completed and the constituent concentrations were noted, the appropriate Water, he weight ratios of oil, surfactant, and co-surfactant were selected.[10]

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(5), 279-291 | ISSN:2251-6727

2.3] Phase diagrams are used to select formulations.

Various formulations from the region of microemulsion were chosen from each diagram of phase that was built with the purpose of incorporate the drug on the bases, into the oil phase listed below. Depending on how well The drug is dissolved in the oil. the concentration of The oil ought to be like this the drug (One dosage) is fully dissolved.

2) To see if the drug had any impact on the microemulsion and phase behaviour region of the phase diagram.

3) The Smix's lowest concentration required for that volume of oil was measured. A number of thermodynamic stability tests were conducted on a choosing of formulations.[11]

Formulations chosen through phase diagrams

Something not the same as was constructed in order to incorporate the drug on the bases, into the oil phase listed below.

1) Depending on how well The medication dissolves in the oil., The concentration of oil need to be such that the medication (one dose) is fully dissolved.

2) To determine whether the drug had an impact during the phase behavior

3) The Smix's lowest concentration required for that volume of oil was measured.

A number of tests of thermodynamic stability were conducted. on a variety of formulations.

Studies of thermodynamic stability

The produced microemulsions thermodynamic stability at different oil mixture and Smix concentrations was tested in order to address the problem of metastable formulations .Initially, microemulsions were filtered based on their thermodynamic stability.[12]

1) Heating cooling cycle

Six cycles between refrigerator temperature (4°C) and (45° C) with storage at each temperature of not less than 48 h was studied. Those formulations, which were stable at these temperatures, were subjected to centrifugation test.

2. Centrifugation:

Following their successful completion of the formulations were subjected to the heating-cooling cycle. centrifugation testing. For 30 minutes, the microemulsions were centrifuged at 3000 rpm. The formulations selected for the freeze-thaw test were those that did not exhibit any phase separation.

3. Cycle of freeze-thaw:

For the microemulsions, Three periods of freezing and thawing from -21°C to +25°C were carried out, with each temperature of storage for each at least 48 hours. The purpose of The purpose of this test was determine the stability of the microemulsions at extremely low temperatures as well as whether freezing would cause them to return to their stable form.

2) Methods

Microemulsion preparation

The drug was weighed precisely (1%w/v) and dissolved in ethyl oleate before Smix was incorporated into the blend. The mixtures that were prepared were mixed together at room temperature using a magnetic stirrer. After that, water was progressively added to the prepared mixture until it was clear and transparent.[13]

Microemulsion characteriszation

1) **Measurement of pH**

An electrode for a pH metre (Lab India, located in Mumbai, India) was directly dissolved at room temperature inside the formulations to determine the pH of the systems. Every measurement was carried out three times.[14]

2)Viscosity

They used a The Brookfield viscometer (DV-II+Pro Brookfield, USA) to calculate the the viscosity of the samples at 25 °CS using spindle number 62 and a shear rate of 150 rpm. Every measurement was made three times[15]

3)Transmittance Measurement

The percent transmittance analysis was used to assess the microoemulsions' clarity. A UV-Vis spectrophotometer (Jasco, Model: V-730) was used for this investigation, and the drug's Lambda max was 251 nm.[16]

Journal of Chemical Health Risks
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JCHR (2025) 15(5), 279-291 | ISSN:2251-6727

3) Determination of drug content

An ultraviolet-visible spectrophotometer (Jasco, Model: V-730, Japan) set to 251 nm was used to measure the drug content of the microemulsions.[17]

4) Particle Size and PDI

The Horiba SZ-100V2 was used to measure these parameters. The instrument used dynamic scattering to determine particle size. In order to achieve uniform dispersion, the dilution was carried out up to ten times using Milli Q water. It was then evaluated at 90◦ at 25 ± 2 ◦C[18]

5) Zeta potential

Using the electrophoretic mobility of the microemulsion under the influence of an electric field, Horiba (SZ-100 series) estimated this parameter. They were added to the chamber after the solution had been diluted with Mili Q water.[19]

In vitro permeation study of microemulsion

The optimized loratadine incorporated microemulsion formulation was used for in vitro permeation profile for topical administration was assessed using a synthetic Strat-M membrane in a Franz diffusion cell setup. This membrane was selected for topical permeation investigations because of its multilayered structure and permeability properties that resemble those of human skin. The donor compartment was filled with the n microemulsion formulation, which contained an equivalent of 10mg/ml entrapped medication. At 37 ± 0.5°C, phosphate-buffered solution (pH 7.4) was added to the receptor compartment as the dissolution medium. To ensure sinking conditions and even mixing, the mixture was constantly stirred with a magnetic stirrer. At intervals of 0, 1, 2, 4, 6, 8, 12, and 24 hours, 1 mL samples were taken out of the receptor compartment and immediately replaced with an equivalent volume of brand-new PBS to maintain a consistent volume. The amount of drug released cumulatively was determined by UV spectroscopy analyzing the extracted samples at the 251 nm in order to calculate the total amount of drug released.[20,21]

FORMULATION OF MICROEMULSION GEL

Optimization of concentration of carbopol 934 for preparation of microemulsion gel of loratadine

The carbopol 934 concentrations used to prepare the microemulsion gel were 0.5, 1.0, and 1.5% w/v. To create a highly viscous solution, the right amount of Carbopol 934 was gradually combined with a small amount of water and left overnight. Next, a microemulsion loaded with loratadine was gradually added to the viscous Carbopol 934 solutions. After employing triethanolamine to bring the pH levels down to 4-6, a microemulsion gel was produced. Based on the microemulsion gel's consistency, the Carbopol 934 concentration was optimised.[22]

Preparation of microemulsion gel of Loratadine

Under stirring, a small amount of water was gradually combined with 1%w/v carbopol 934.For full swelling, the gel was left overnight. Drop by drop, triethanolamine was added to the gel to bring its pH down to about 5-7. Then, a glass rod was used to thoroughly mix an equal amount of microemulsion and gel (1:1)

Preparation of control Loratadine gel

Take charge in order to create loratadine gel, 1%w/v 934 carbopol was dissolved in an adequate amount of filtered water. The carbopol 934 solution was allowed to fully swell overnight following dispersion. Next, enough methanol was added to dissolve the loratadine, this drug solution was gradually added to the carbopol 934 aqueous dispersion. Following that, a triethanolamine solution was used to bring the pH down to 4-6 in order to produce Loratadine gel.

Evaluation of Gel Based on Microemulsion

Determination of pH

The microemulsions' pH values were quantified. with a digital pH meter. [23]

Viscosity

A Brookfield digital viscometer (Brookfield (DV-II+Pro) U.S.A.) was used to measure the microemulsion's viscosity. At 50 rpm, No. C was utilised

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(5), 279-291 | ISSN:2251-6727

with a T-shaped spindle. [24]

Determination of drug content

A UV-visible spectrophotometer is used to determine the drug content of, the microemulsions at 251 nm. (Jasco, Model: V-730, Japan) [25]

Spreadability

Glass plates measuring were used to examine the sample's spreadability. In the center of the initial glass slide, put required amount of the microemulgel. To create a thin layer of microemulgel between the two glass slides, carefully place the second one on top of the first. To guarantee even spreading, place known standard weight on the top slide for few minutes.Use a ruler to measure the spread microemulgel's diameter after the weight has been removed.[26]

Permeation study in vitro

In vitro permeation study was performed to assess the topical delivery potential of the Loratadine loaded microemulgel formulation by utilizing a Franz diffusion cell system. Strat-M synthetic membrane was employed as the diffusion barrier based on its multilayered structure and permeability profile closely resembling human skin, rendering it suitable for modeling in vivo conditions. An amount of 2gm of the Loratadine loaded microemulgel preparation, equivalent to 10 mg of drug, was cast evenly on the donor compartment of the Franz diffusion cell. The receptor compartment was loaded with phosphate-buffered saline (PBS, pH 7.4) at a temperature of 37 ± 0.5°C to mimic skin surface conditions. The receptor fluid was stirred constantly with the aid of a magnetic stirrer to ensure homogeneity and sink conditions throughout the experiment. 1-mL samples were removed from the receptor compartment at preselected time intervals (e.g., 0, 1, 2, 4, 6, 8, 12, upto 24 hours) and refilled instantly with fresh PBS to provide a constant volume and concentration gradient. The harvested samples were measured using a validated UV-Visible spectrophotometric assay to quantify the quantity of drug permeated through the membrane.[27]

Study of permeation mechanism by curve fitting

The best fit models, which include The Higuchi release, the Korsmeyer Peppas model model, first order, and zero order were identified by fitting permeability data to a variety of mathematical models.[28]

Stability study

The purpose of the stability study was to confirm the formulation's chemical and physical integrity. A stability analysis was performed on the optimised microemulsion-based gel. Storage conditions were maintained in accordance with the International Conference of Harmonization's (ICH) recommendations. For During the real-time study, 25 ± 2 C and 60 ± 5% RH were utilised for a month, and 40 ± 2 C and 75 ± 5% RH were used for the accelerated stability study.[29]

Results and discussion

Drug Characterization

Loratadine was a solid white powder with a melting point of 132-137°C.

Screening of Oil, Surfactant and Cosurfactant

Among the screened Co-surfactants, oils, and surfactants, loratadine demonstrated good soluble in propylene glycol, tween 20, and ethyl oleate. In order to create the microemulsion, they were further chosen. The solubility of loratadine in methanol.

Solubility Study of loratadine

Table 1 shows how loratadine dissolves in a range of oils, cosurfactants, and surfactants.

Solubility Table :1 of loratadine in oils

Sr.no	oils	Solubility (mg/ml) mean ± SD
1	Orange oil	5.436 ±0.678
2	Ethyl oleate	12.719 ±0.709
3	Lemon grass oil	7.787 ±0.760
4	Seasame oil	8.2667 ±0.0981
5	Clove oil	5.034 ±0.462
6	Isopropyl myristate	11.340±0.557

Journal of Chemical Health Risks
www.jchr.org
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7	Castor oil	4.672 ±0.664
8	Cinnamon oil	5.320 ±0.688

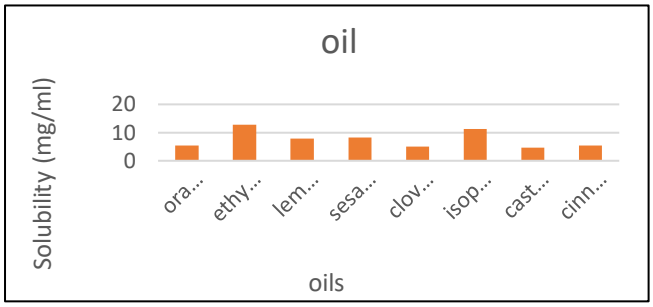

Figure 1: Data of oil solubility study of loratadine

Table no: 2 Solubility of loratadine in Surfactants and Cosurfactants

Sr.no	Surfactants and, cosurfactants	Solubility (mg/ml) mean ± SD
1	Tween 20	10.891±0.554
2	Tween 80	9.530±0.549
3	Tween 40	4.465±0.679
4	Ethanol	10.201±0.935
5	PEG 200	9.923±0.462
6	PEG 400	7.892±0.588
7	Propylene glycol	14.284±0.723

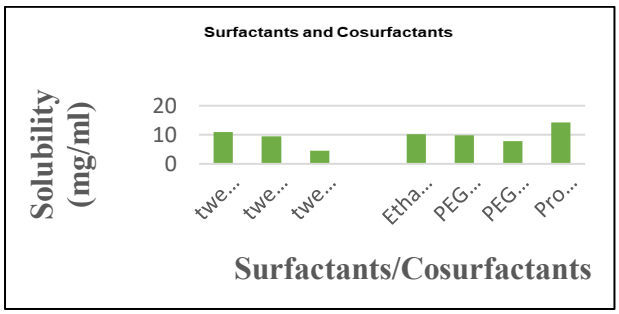

Figure 2: Data of surfactant, cosurfactant

Construction of Pseudoternary phase diagram

Phase diagrams were created using various Smix ratios (Tween 20: Propylene glycol), such as Figure 3,4,5 shows 1:1, 2:1, and 3:1. The O/W microemulsion's region that has the components' intended concentration range (Oil, Smix, and Water) was aided by these phase diagrams.

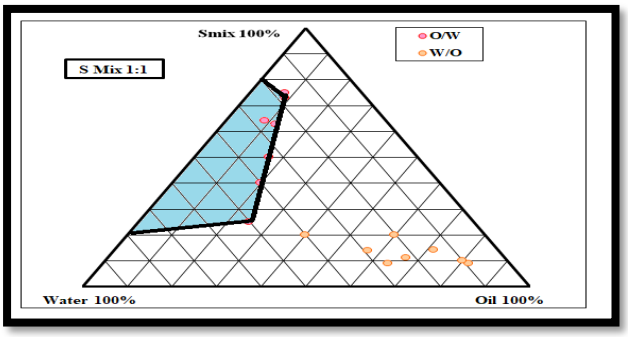

Fig no:3 Microemulsion regions of ratio 1:1

The Smix (Tween 20: Propylene glycol) microemulsion region is depicted in this diagram in a 1:1 ratio.Water, oil (ethyl oleate), and Smix are all 100% represented by the triangle corners.The region that formed stable O/W microemulsions is indicated by the blue-shaded area.Systems that are water-in-oil (W/O) or oil-in-water (O/W) are indicated by orange dots and pink dots, respectively.Only formulations that were stable, clear, and chosen for additional development fell into the blue area. Finding the ideal ratios of water, oil, and surfactant was made easier by this diagram.

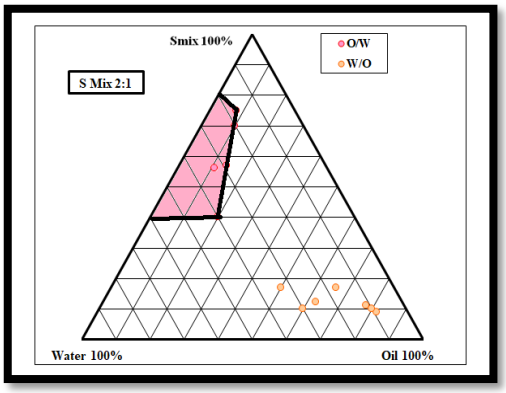

Fig no:4 Microemulsion regions of ratio 2:1

The microemulsion region for Smix (Tween 20: Propylene glycol) in a 2:1 ratio is depicted in this diagram.100% Smix (top), 100% water (left), and 100% oil (right) are indicated by the triangle corners.The region where O/W (oil-in-water) microemulsions formed is indicated by the pink shading.Orange dots show unstable

W/O (water-in-oil) systems, whereas pink dots show stable O/W systems.The microemulsion region grew

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(5), 279-291 | ISSN:2251-6727

when the surfactant concentration was increased to 2:1 as opposed to 1:1.This Smix ratio was appropriate for drug delivery systems because it provided better emulsification and stability.

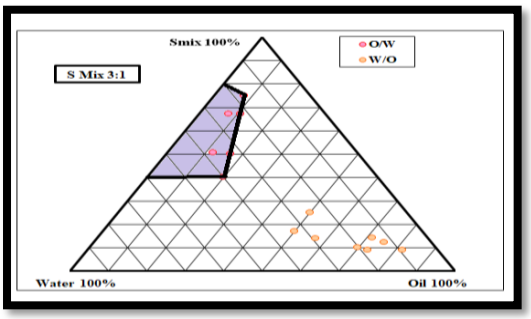

Fig no:5 Microemulsion regions of ratio 3:1

this diagram.The corners of the triangle stand for water on the left, oil on the right, and 100% Smix on the top.The region where O/W microemulsions were successfully formed is indicated by the purple shading.Stable oil-in-water (O/W) systems are indicated by pink dots, while unstable water-in-oil (W/O) systems are indicated by orange dots.The microemulsion region is present, but it is somewhat diminished in comparison to the 2:1 ratio.Thermodynamic stability studies.

Results from Table 3 analysis of a few chosen formulations from Phase Diagrams A, B, and C are shown. Stability test-passing formulations were selected regarding size analysis. Centrifugation analysis.The stability tests that were conducted included cycles of heating, cooling, and freezing and thawing.

Table no 3 thermodynamic stability tests for different formulations chosen from the phase diagram.

Percentage (v/v) of different components					**observation based on thermodynamic stability study**			
Phase diagram	**T20/Propylene glycol**	**Oil**	**Smix**	**Aqueous**	**H/C**	**Cent**	**Freez. Thaw**	**Inference**
A	1:01	10	70	20	✓	✓	✗	Failed
A	1:01	10	60	30	✓	✓	✓	passed
A	1:01	10	50	40	✓	✓	✓	passed
A	1:01	10	40	50	✓	✗	_	Failed
A	1:01	10	30	60	✗	_	_	Failed
B	2:01	10	70	20	✓	✓	✗	Failed
B	2:01	10	60	30	✓	✓	✓	passed
B	2:01	10	50	40	✓	✓	✓	passed
B	2.1	10	40	50	✓	✗	_	Failed
C	3:01	10	70	20	✓	✓	✗	Failed
C	3:01	10	60	30	✓	✓	✓	passed
C	3:01	10	50	40	✓	✓	✓	passed
C	3:01	10	40	50	✓	✗	_	Failed

EVALUATION OF MICROEMULSION

pH and Viscosity

All microemulsion formulations had a pH between 4.76±0.59 and 5.76±0.17, which is comparable to the pH of the skin's surface. These formulations' viscosities ranged from 33.00±1.0 to 47.66±0.57 The F2 formulation's pH and viscosity were determined to be 5.46±0.376 and 43.66±1.52, respectively.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(5), 279-291 | ISSN:2251-6727

Drug content and % of Transmittance

The formulations' drug contents varied ranging from 95.75±0.39 to 98.54±0.39, and their transmittance percentages fell between 94.31±0.0421to 98.982±0.333 . The F2 formulation's drug content and transmission percentage were determined to be 97.64 ± 0.35 and 98.982 ± 0.333, respectively.

Particle size and PDI

The formulations were found to have a polydispersity index of 0.362 to 0.411 a particle size of 76.5 nm to 195.2 nm, which was closer to the typical microemulsion particle size of 10-200 nm.

Zeta potential

(Figure 6). The formulations' The zeta potential ranged from -19.1 mV to -32.4 mV. The worth of the zeta potential of stable microemulsion systems were generally greater than ± 20 mV. The stable microemulsion was indicated by the F2 formulation based on the zeta potential value and particle size.

Table no4 :Physical Characteristics of microemulsion Formulations (Mean ± SD)

ratio	Batch	%T	pH measurement	Viscosity	Drug content	Particle size (d.nm)	Polydispersity index	Zeta potential (mV)
1:01	F2	98.982±0.333	5.46±0.376	43.66±1.528	97.64±0.35	76.5 nm	0.411	-32.4
	F3	94.58±0.295	5.76±0.173	33.00±1.000	98.54±0.39	104.3 nm	0.348	-25.7
2:01	F7	97.169±0.792	5.30±0.273	45.66±1.528	96.27±0.30	102.1 nm	0.363	-29.8
	F8	94.31±0.0421	5.46±0.376	36.66±1.528	95.75±0.39	88.8 nm	0.363	-30.4
3:01	F11	95.765±0.150	5.30±0.273	47.66±0.577	97.53±0.37	120.7 nm	0.37	-22.9
	F12	90.69±2.78	4.76±0.593	38.00±1.00	96.83±0.40	195.2 nm	0.362	-19.1

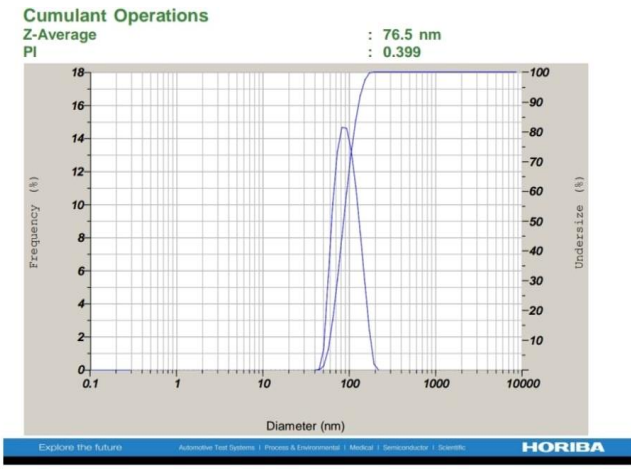

Fig 6 : Particle size

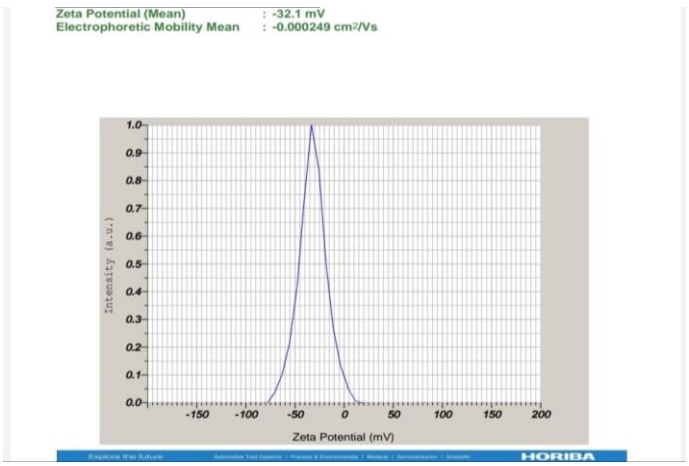

Fig 7 : Zeta potential

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(5), 279-291 | ISSN:2251-6727

Formulation of microemulgel Optimization of concentration of carbopol 934 for preparation of microemulsion gel of loratadine:

Carbapol 934 was chosen as the gel matrix to produce the gel based on microemulsion formulation. The The consistency of the microemulsion gel was used to optimise the carbopol 934 concentration.. The fluidity of a microemulsion gel containing 0.5 and w/v carbopol 934 was relatively high. However, adding 1.5% w/v carbopol 934 resulted in a very viscous mcroemulsion gel. The microemulsion gel with Carbopol 934 at 1%w/v had a consistency that was almost perfect for transdermal application. 1%w/v To prepare the microemulsion gel formulation, carbopol 934 was chosen as the gel matrix.

Preparation of microemulsion gel of loratadine and control loratadine gel

Loratadine microemulsion gel and control gel are made in accordance with the documented protocol.

Evaluation of Microemulgel

pH

The pH of the F2 microemulgel was found to be 5.92 ± 0.28 which is similar to the pH of skin surface, that might prevent the occurrence of any irritation or caustic reaction.

Viscosity

Viscosity of microemulgel of F2 batch was found from 15636±1.74

Determination of drug content

The drug content of F2 formulation was determined to be 97.26 ± 0.14 respectively.

Spreadability

Spreadability of F2 formulation was found to be 6.5 ± 1.39 indicating good spreadability

(Table 5).

Table no 5. Evaluation of microemulgel.

Batch	pH	Viscosity (cP)	Drug content (%)	Spreadability(cm)
F2	5.92±0.28	15636±1.74	97.26±0.14	6.5±1.39

In Permeation was studied in vitro.

In a 24-hour period, the cumulative percentage of drug penetration for the microemulsion, microemulgel, and control gel is 91.710± 1.093, 82.810± 0.609, and 35.097± 0.657, respectively.The microemulsion shows the highest percentage of drug penetration when compared to the control gel and microemulgel. Consequently, the loratadine-loaded microemulgel showed sustained release over the proper time frame.This happened because a microemulsion was added to the gel, acting as a barrier to delay the formulation's molecules' release.vitro study of permeation.

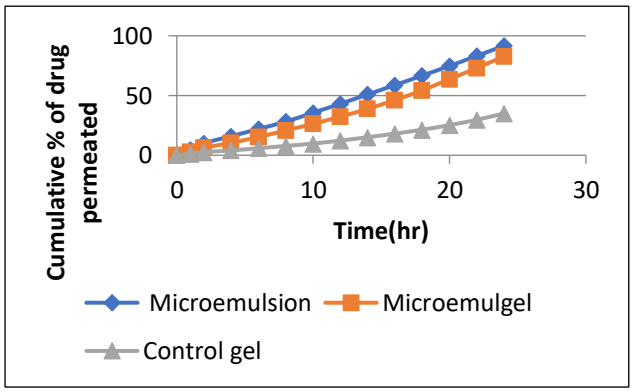

Fig.6 Cumulative % of drug permeated

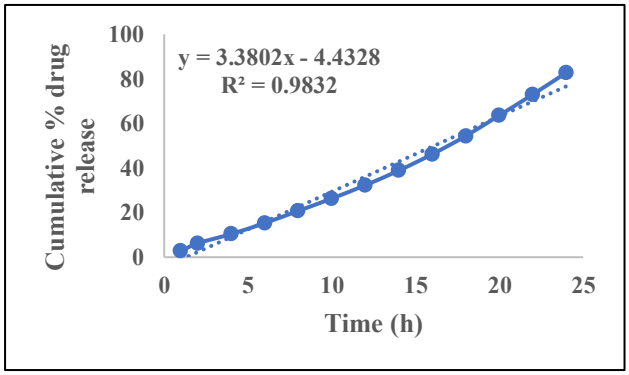

Fig.7: Zero order

Journal of Chemical Health Risks
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JCHR (2025) 15(5), 279-291 | ISSN:2251-6727

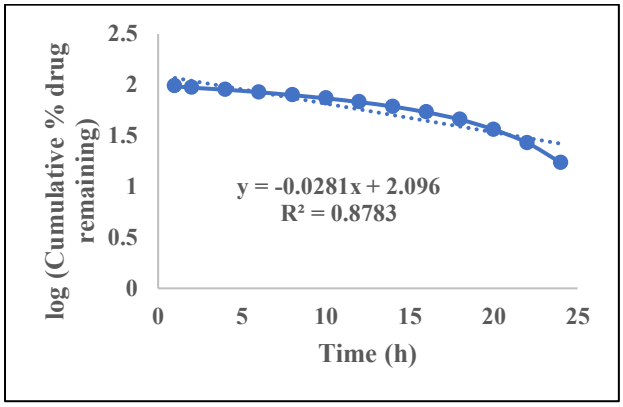

Fig.8: First order

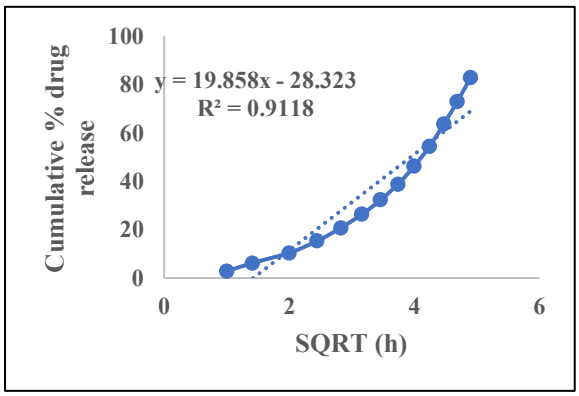

Fig.9: Higuchi model

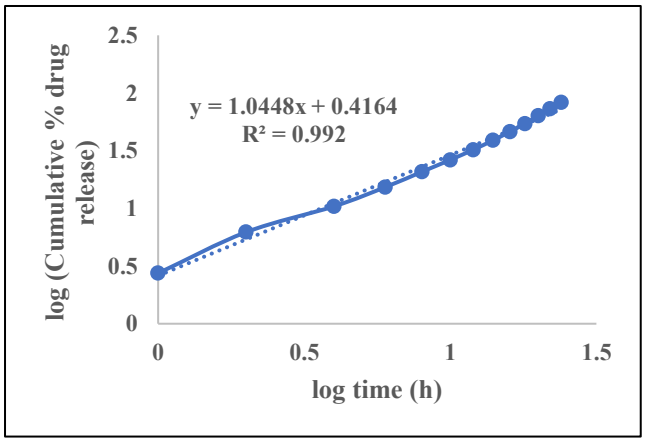

Fig.10: Korsmeyer Peppas model

According to the The drug release from the Korsmeyer-Peppas model microemulgel the best, with the highest R2 value. This indicates that rather than relying solely on diffusion, the drug release is governed by a complex mechanism that involves polymer swelling and relaxation.Thus, this model provides the best explanation for the drug's gradual release from the formulation.

Table:6 The table interpreting drug permeation kinetics of F3 formulation formulated in microemulgel

Kinetics Model	Equation	R^2 value	Fit Quality	Mechanism Type
Zero-Order Kinetics	$Qt=k0.t$	0.9832	Good fit	Constant release
First Order Kinetics	$Qt=Q\infty\cdot(1-e^{-k\cdot t})$	0.8783	Poor fit	Concentration-dependent
Higuchi Model	$Qt=kH.\sqrt{t}$	0.9118	Moderate fit	Diffusion-controlled
Korsmeyer-Peppas Model	$Qt=kKP.t^n$	0.992	Excellent fit	Super Case-II

Stability study:

The table shows the findings of a one-month stability study.

Table no:7 Impact on the evaluation parameter following a sample stability study.

Evaluation parameters	Initial (Day 0)	After 1 month (25 ± 2° C, 60 ± 5 %RH)	After 1 month (40 ± 2° C, 75 ± 5 %RH)
Physical appearance	Smooth and white	Smooth and white	Smooth and white
pH	5.92±0.28	5.86±0.18	5.75 ±0.15

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(5), 279-291 | ISSN:2251-6727

Viscosity (cps)	15636±1.74	15490 ±2.10	15120 ±2.50
Drug content (%)	97.26±0.14	96.85 ±0.20	96.20±0.30

The loratadine-loaded microemulgel maintained its physical integrity, viscosity, pH, and drug content after a month of storage both in standard (25°C/60% RH) and accelerated (40°C/75% RH) conditions, suggesting that the formulation is both chemically and physically stable.

Conclusion:

A loratadine-loaded microemulgel for topical use was effectively created in this study.Transdermal delivery was used to overcome loratadine's poor oral bioavailability and first-pass metabolism. For the best solubility and microemulsion formation, propylene glycol, Tween 20, and ethyl oleate were selected. The microemulgel's consistency and usability were improved by using a 1% Carbopol 934 gel. Formulation F2 had a good drug content (97.26 ± 0.14%) and a pH of 5.92 ± 0.28, which is suitable for skin. Easy application on the skin was guaranteed by its good spreadability (6.5 ± 1.39 cm). Compared to the control gel (35.09%), in vitro permeation demonstrated a drug release of 82.81% over a 24-hour period. Super Case-II transport was indicated by drug release that adhered to the R2 = 0.992 Korsmeyer–Peppas model. This points to a combination of gel relaxation-controlled release and diffusion. Studies of stability. No significant changes in pH, viscosity, or drug content were confirmed by studies conducted under ICH conditions. The sustained release profile of microemulgel was comparable to that of microemulsion alone (91.71%). The formulation effectively by passes first-pass metabolism, improving therapeutic efficacy. It combines the advantages of gel (viscosity and stability) and microemulsion (penetration). An efficient, reliable, and patient-friendly substitute for oral loratadine is provided by this system. All things considered, the microemulgel is a promising non-invasive method of treating allergic skin conditions.

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