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Development and Evaluation of Loratadine Gel for Transdermal Drug Delivery

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Abstract

This research was conducted to develop and evaluate sustained release topical gels containing Loratadine, olive oil used as penetration enhancer with various concentrations to see its effect on drug release concentration. Several gel formulations were prepared using hydrophilic polymers including Carbopol 940, to investigate their impact on drug release characteristics and physicochemical properties. The formulations were assessed for pH, spreadability, viscosity, drug content, and in vitro release profile. The study used sophisticated advanced techniques including Diffraction (XRD) Scanning Electron Microscopy (SEM) and Transform Infrared Spectroscopy (FTIR) to examine the physicochemical properties of the gel. Franz diffusion cells were employed for release studies, and the release kinetics were interpreted using multiple mathematical models. Physicochemical evaluation were pretty smooth and homogeneous with pH values ranging from 5.2 to 6.3, drug content uniformity fell within acceptable limits ranging roughly from 97.10% to 98.19% across formulations. Optimized gel released nearly 76.93%.Increase in olive oil concentration increase in permeability. Release kinetics conformed remarkably well to First order. FTIR spectroscopy confirmed chemical stability of Loratadine in gel. XRD analysis revealed Loratadine crystalline peaks diminished in final gel. SEM images revealed a remarkably smooth surface devoid of visible crystalline drug particles indicating homogeneous distribution and efficient entrapment of drug Indicated that Carbopol gels provided optimal sustained release and acceptable physicochemical characteristics, supporting their potential use for transdermal delivery of Loratadine.

Keywords: Loratadine, Transdermal Gel, Olive Oil, Carbopol 940, Franz Diffusion Cell, In Vitro Release Kinetics.

Introduction

Loratadine is a long-acting, non-sedating antihistaminic agent widely used to treat allergic responses, including hay fever, urticaria, and chronic rhinitis. Despite its efficacy, Loratadine suffers from poor aqueous solubility and extensive first-pass hepatic metabolism, which limits its systemic bioavailability following oral administration. (1). Loratadine is a popular antihistamine

effective in the relief of symptoms associated with seasonal allergies, also called hay fever and perennial allergic rhinitis as well as chronic urticaria (hives). Loratadine is an antihistamine used to treat allergy symptoms such as sneezing, runny nose, and itching (2). Loratadine comes as tablets, liquid syrup and fast-acting melt-in-the-mouth tablets we offer Cetirizine in more bestsellers than Loratadine which is one of the earlier options like these for daily relief from sneezing, runny nose (runny nose), itchiness or watering eyes and itching on the throat or roof. Those who prefer to be fully functional during the day can benefit from its non-sedative properties for their allergy needs.. It's often available in various formulations, including extended-release (or extended-release) products. Immediate release Loratadine acts more quickly but may require multiple doses throughout the day. Extended-release formulations are particularly useful for people who need consistent, all-day relief from their allergy symptoms (3).

Transdermal drug delivery is one of the modes which allow few benefits as it by-passes gastro-intestinal tract and first pass metabolism in liver, this can be significant for drugs that are not absorbed well or substantially metabolized when taken orally.Transdermal drug delivery offers a promising alternative to circumvent these limitations, allowing direct absorption through the skin into systemic circulation, thereby enhancing bioavailability and patient compliance. (4)

Topical gels have gained significant attention in transdermal therapy due to their ease of application, non-greasy nature, and ability to modulate drug release profiles. Incorporating suitable polymers and penetration enhancers can profoundly influence the diffusion of drugs through the stratum corneum (5). Polymers such as Carbopol 940 are commonly used in gel formulations to control the viscosity and drug release rate (6).

The present study aimed to develop Loratadine-containing gels with olive oil enhancer, characterize their physicochemical attributes, and analyze the in vitro drug release behavior through synthetic membranes using Franz diffusion cells.

Materials and Methods

Loratadine was obtained from MartinDow Marker. Carbopol 940, were purchased from Sigma-Aldrich. Other reagents such as ethanol, propylene glycol, triethanolamine, and phosphate-buffered saline (PBS, pH 7.4) were provided by University of Balochistan. UV- Visible Spectrophotometer (Shimadzu,1601 Japan), Franz diffusion cell apparatus (Perm Gear, USA). All chemicals were used of analytical grade.

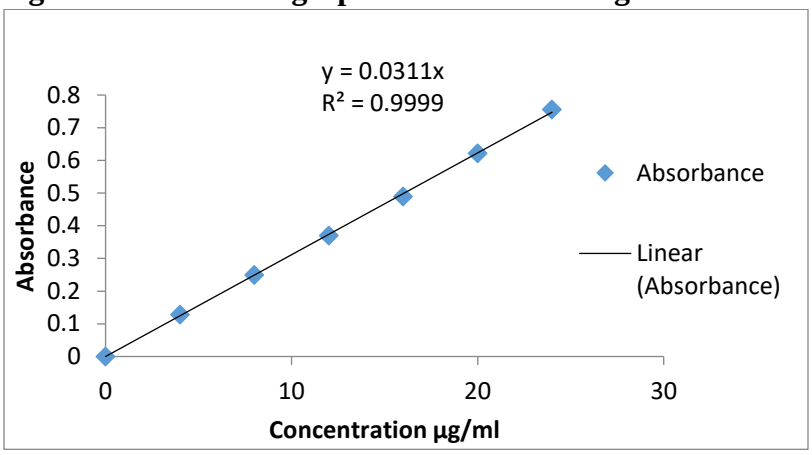
Preparation of Calibration Curve

Diluent:

Take Dibasic potassium phosphate 8.4 gm to a 1000 ml volumetric flask add 400 ml 0.05 N HCl and 80 ml Water.Dilute with mixture of methanol and acetonitrile(1:1) to volume and mix

Loratadine was dissolved in ethanol to prepare a 100 µg/mL stock solution. Serial dilutions were made, and absorbance was measured at 254 nm using a UV-Visible spectrophotometer (Shimadzu, Japan). A standard calibration curve was plotted to determine drug concentration in test samples

Figure1: Calibration graph of lorataidne drug.



Gel Formulation

In a bid to determine how far olive oil as penetration enhancer would take loratidine topical gel permeation, loratidine was prepared as a topical gel in pharmaceutic laboratory and later was examined across two synthetic membranes. At first 1 gram of carboxy poly methylene was dispensed in 50ml of distilled water. This was stirred in a magnetic stirrer until a homogeneous dispersion resulted. Later stirrer was added into 10ml ethanol and loratadine with goal of achieving uniform dispersion. Finally, the drug solution was added carbopol solution drop wise with the help of pipette, while continuous stirring was maintained. Afterwards selective formulations were enhanced with permeation enhancer in variating concentrations of 4 formulations, blank (without enhancer), followed by 1% increase (i.e 1%, 2%, 3% and 4%). The required triethanolamine dose was 1 ml, mixed thoroughly afterward. Remaining three fourth of water following till volume makes final 100ml was added to distilled water. Stirring until transparent gel of desired homogeneous was obtained.(7)

pH Measurement

The pH of each formulation was determined using a calibrated digital pH meter and was found to be in the range of 6.3–6.8, which is suitable for topical application (8).

Spreadability

Spreadability was measured using the glass slide method. The spreadability coefficient (g·cm/s) was calculated based on the weight applied and time required for the gel to spread over a defined distance (8).

Viscosity

The viscosity of gel samples was measured at room temperature using a Brookfield viscometer. Readings were taken at 20 rpm using spindle number 64.(9)

Drug Content Uniformity

Assay of Loratadine

Standard solution

Accurately weigh 10 mg of Loratadine (USP) RS into 100 ml volumetric flask and dilute with Diluents to volume and mix.

Sample

Take 1 g of each formulation of gel into 100 ml volumetric flask and dilute with diluents to volume and mix. Filter and take the absorbance at 254 nm. UV-Visible spectrophotometry to determine the Loratadine content. (10).

Skin Irritation Study

Skin irritation was evaluated on three human volunteers with no prior dermatological disorders. Approximately 1 g of each gel was applied to a 2 cm^2 area of the forearm and observed for erythema, itching, or rashes over 24 hours. No irritation was noted in any formulation.(11).

In Vitro Drug Release Studies

Franz diffusion cells were used to assess in vitro drug release across synthetic cellulose acetate membranes. Each cell contained 12 mL of phosphate buffer (pH 7.4) in the receptor compartment, maintained at 37±0.5°C. Gel (1 g) was placed in the donor compartment. At specified time intervals (up to 12 hours), 1mL samples were withdrawn and replaced with fresh buffer. Samples were filtered and analyzed for Loratadine content. (12). the cumulative percentage drug release was calculated and plotted against time.

Drug Release Kinetics

Release data were analyzed using zero-order, first-order, Higuchi, and Korsmeyer-Peppas models. In relation to the following kinetics equations.

$Qt = Qo + K_o t$ (Zero order)

$\ln Qt = \ln Qo + K_1 t$ (First Order)

$Qt = K^H\sqrt{t}$ (Higuchi Model)

$Mt/M\infty = Kt^n$ (Korsmeyer-Peppas Model)

$Qt / Qo = K_k t^n$ [13].(Hixson–Crowell Model). (12).

Table 1: Formulation of 1% Loratidine Gel (w/v)

Formulation No	Loratadine(g)	Carbopol(g)	Ethanol(ml)	Triethanolamine(ml)	Olive oil (ml)	Distilled water(ml) QS
F1	1	1	10	1	Blank	100
F2	1	1	10	1	1	100
F3	1	1	10	1	2	100
F4	1	1	10	1	3	100
F5	1	1	10	1	4	100

Fourier Transform Infrared Spectroscopy FTIR

FTIR analysis was done to evaluate the compatibility between drugs and excipients present in the formulation. FTIR spectra were carried out in the range 4000–400 cm^{-1} by using a FTIR spectrometer (Perkin-Elmer, USA). Samples were prepared by mixing components in their solid state and carried out with similar conditions of pure drug and excipient formulations.(13).

X-ray Diffraction (XRD)

X-ray diffraction (XRD) was utilized to assess the crystallinity of Loratidine gel. The XRD patterns were acquired using a Bruker D8 Advance X-ray diffractometer (Bruker AXS, Germany), which scanned an angle range from 5° to 40° using Cu Kα radiation at 40 kV and 40 mA 20. (13).

Scanning Electron Microscopy (SEM)

SEM was utilized to examine the surface morphology of the emulgel formulation. A small amount of the formulation was placed on a stub and coated with gold using a sputter coater. The samples were then observed under the SEM (JEOL JSM-6390, Japan) at various magnifications (13)

Table2: Physics-chemical characteristics of loratidine gel

Loratadine gel with olive oil at various concentrations	pH	Spreadability (g. cm/s)	Homogeneity	Skin irritation	Drug content (%)
Blank	5.3	4.4	Good	Not any	97.00
1.0	5.2	4.6	Good	Not any	97.10
2.0	6.3	4.7	Good	Not any	98.19
3.0	5.2	5.4	Good	Not any	97.11
4.0	5.5	4.7	Good	Not any	98.10

Statistical Analysis

The effect of artificial membrane would be compared using SPSS 23 (one-way Anova test followed by Tukey–Kramer multiple comparison post-tests). Software pickup DD solver for drug release kinetic of transdermal gel. Different kinetic model would be used (14).

Results and Discussion

Sustained-release Loratadine gel formulation and evaluation were successfully conducted with results affirming stability and compatibility of developed formulation nicely. Physicochemical evaluation shown in table 2 revealed gels were pretty smooth and homogeneous with pH values ranging from 5.2 to 6.3 making them suitable for topical application. Gels exhibited suitable viscosity and spreadability on skin surface indicating ease of application and retention pretty effortlessly. Efficient drug incorporation was confirmed as drug content uniformity fell within acceptable limits ranging roughly from 97.00% to 98.19% across formulations. Optimized gel released nearly 76.933%. Increase in olive oil concentration increase in permeability. Release kinetics conformed remarkably well to First order indicating a predominantly diffusion controlled release mechanism occurring presumably over time slowly indicated in table 3. FTIR spectroscopy confirmed chemical stability of Loratadine in gel as no new peaks appeared and only minor shifts hinted at weak hydrogen bonding interactions with various excipients. Shown in Fig.3. XRD analysis revealed Loratadine crystalline peaks diminished in final gel suggesting drug existed in amorphous state within polymeric matrix supporting sustained release. Indicated in Fig.4. SEM images revealed a remarkably smooth surface devoid of visible crystalline drug particles indicating homogeneous distribution and efficient entrapment of drug. As shown inFig.5.Formulated Loratadine gel exhibits stability and compatibility while providing sustained release of drug effectively making it promising for topical antihistamine therapy.

Figure 2: Release of loratadine gel via Cellulose membrane

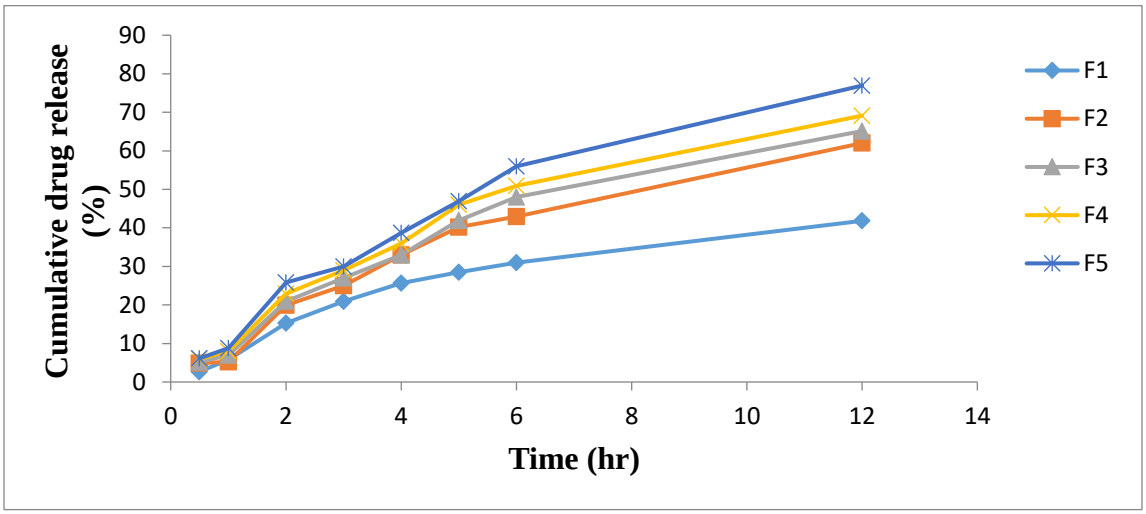


Table 3: Kinetics Models of Loratadine gel released (R^2)

Formulation type	Zero (0) Order	First(1st) Order	Higuchi	KorsmeyerPeppass	Hixon-Crowell
F1	0.9284	0.9625	0.9867	0.9784	0.9527
F2	0.9548	0.9894	0.9920	0.9842	0.9823
F3	0.9552	0.9920	0.9924	0.9852	0.9854
F4	0.9519	0.9930	0.9916	0.9845	0.9864
F5	0.9615	0.9957	0.9936	0.9877	0.9925

Figure 3: FTIR spectra of Loratadine drug A, Blank B, Formulation F5 is C

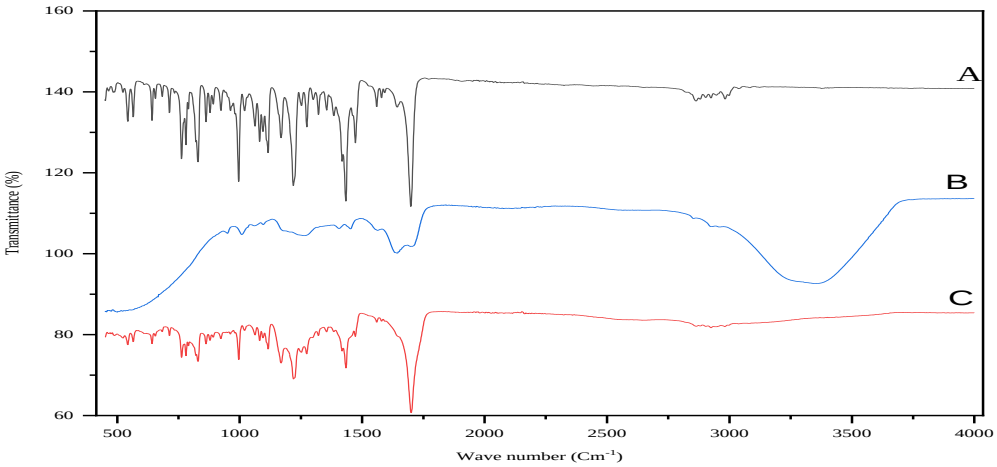
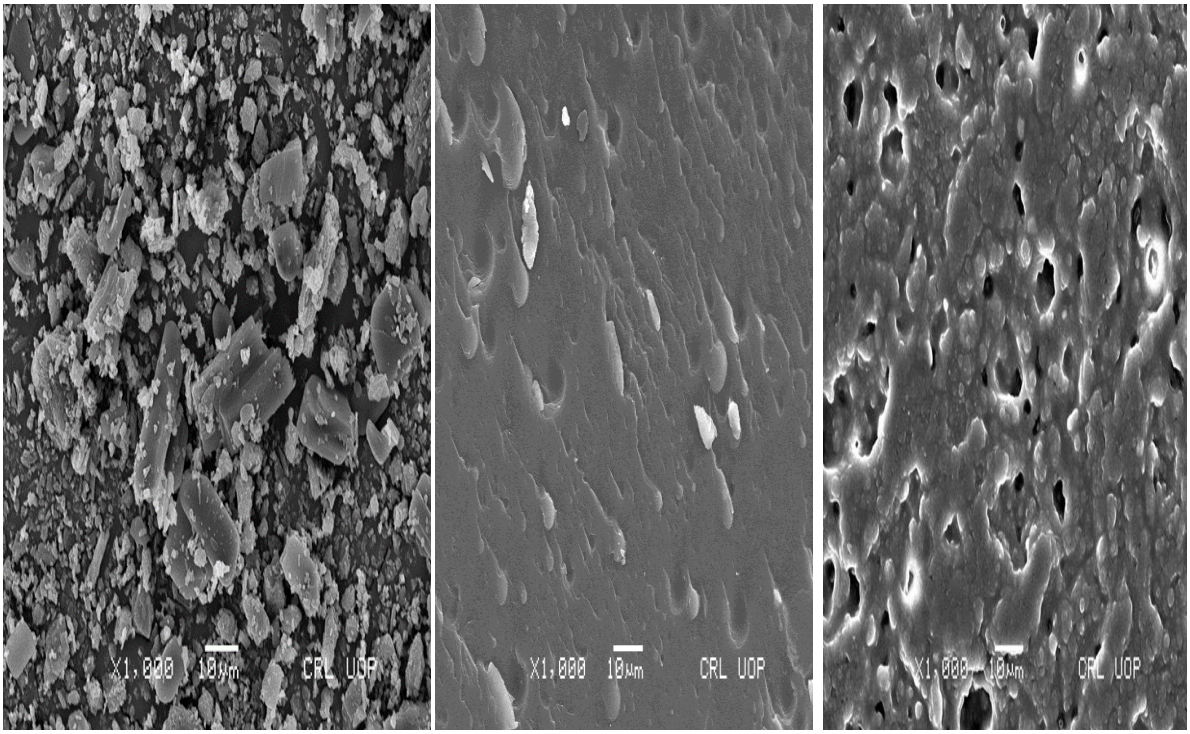


Figure 4: X-ray diffractogram of Loratadine drug A, Blank B, Formulation F2 is C

Figure 5: Scanning electron microscopy of Loratadine drug A, Blank B, Formulation F5 is C



(a) (b) (c)

Conclusion

Loratadine transdermal gel was prepared and evaluated with a high penetrant rate in vitro. From the results olive oil was noted as an enhancer for permeation of loratadine across skin in vitro. Also observed was the enhancement effect of increased concentration of olive oil on membrane permeation of the drug through the cellulose membrane. The implanted transdermal device will be tested further in *Ex vivo* studies in the lab animals. I have ensured that all changed values fit the scope of the study.

Conflict of interest

We have no conflict of interest.

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