

*Full Length Research Paper*

# Development of oral strip for Loratadine and in vitro evaluation

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Loratadine is a second-generation histamine H1 receptor antagonist used in the treatment of allergic rhinitis and urticaria. The present work was aimed to develop of Loratadine using HPMC E15 LV PREMIUM as film forming polymer, glycerin as a plasticizer and tween 80 as a surfactant. The strips were evaluated for thickness, tensile strength, % elongation, disintegration time and in vitro drug release. A trial and error approach was used in present study for optimization. Oral strip containing HPMC E15 LV PREMIUM (190 mg), tween 80 (15% of polymer) and glycerin (20% of polymer) has given the maximum in vitro drug release and imparts good transparency. A satisfactory result in the strip was exhibited in the way of in vitro release that came in 20 minutes. The drug excipients compatibility study showed that there were no interaction between drug and excipients. Stability study of the optimized formulation showed that the strips were stable at accelerated environmental conditions. Before, the DSC data showed no crystalline form but after 1 month short term, accelerated stability study showed that there was partial crystallization but no change in in vitro dissolution study. So it was concluded that the prepared dosage form was suitable for oral drug delivery.

**Key words:** Oral strip, solvent casting, disintegration time, loratadine, transparency.

## INTRODUCTION

Pharmaceutical dosage forms are normally administered in the form of pills, granules, powders and liquids. Normally, a pill is design for swallowing intact or chewing to deliver a precise dosage of medication to patients. The pills including tablets and capsules are able to retain their shape under moderate pressure. However, patients particularly pediatric and geriatric have suffered difficulty in swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are facing problems to take these solid preparations due to fear of choking.

In order to assist these patients, several fast-dissolving drug delivery systems have been introduced into the market (Arya A, 2010). Oral route is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in formulations. In a recent scenario many researchers and scientist have developed their mind to new drug delivery

system. One such relative dosage form is oral strip drug delivery system. Oral strip is made up of hydrophilic polymers that rapidly dissolve on buccal cavity or on the tongue (Cilurzo F, 2008).

Loratadine is a derivative of azatadine and a second-generation histamine H1 receptor antagonist used in the treatment of allergic rhinitis and urticaria (Dixit RP 2009). Unlike most classical antihistamines (histamine H1 antagonists) it lacks central nervous system depressant effects such as drowsiness. Loratadine competes with free histamine and exhibits specific, selective peripheral H1 antagonistic activity (DB00455, 2012; Gopal V, 2011; Popavic G, 2009). This block the action of endogenous histamine which subsequently leads to temporary relief of the negative symptoms (For example: nasal congestion, watery eyes) brought on by histamine. Loratadine has low affinity for cholinergic receptors and does not exhibit any appreciable alpha-adrenergic blocking activity in-vitro. (Jalil A 2010). Loratadine also appears to suppress the release of histamine and leukotrienes from animal mast cells and the release of leukotrienes from human lung fragments, although the clinical importance of this is

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unknown (Kulkarni PK 2011; Lec ST, 1991). Strip is one of the alternative routes of administration to avoid first pass metabolism and provide immediate action. The present study was aimed to formulate oral strip of Loratadine and evaluate its physicochemical properties and in vitro drug release.

## MATERIALS AND METHODS

### Materials

Loratadine was obtained as a gift sample from the institute of Nivika Chemo-PharmaPvt Ltd, Ankleshwar, India. And all other materials were purchased from local market by the institute.

### Methods

#### Preparation of Loratadine oral strips

Strips were prepared by using different grades of hydroxyl propyl methyl cellulose by casting method (Lutfulkabar AK, 2009). In the preliminary screening three different grades of HPMC such as E5, E15 and E50 were used to formulate strips and E15 was selected due to the less brittleness of the strip. Then glycerin (20% of polymer) was selected as plasticizer amongst tri-ethyl citrate, castor oil, propylene glycol, PEG 200, PEG 400, PEG 600 due to its higher plasticity. Then tween 80 was selected as a surfactant of 15% of polymer due to more transparency. Thus the final formula was introduced, the formation of oral strip (Loratadine). The specified amount of HPMC E 15 was weighed and dissolved in 7 ml of ethanol and 3 ml of dichloromethane mixture. An increase in the quantity of aspartame, glycerin and tween 80 was added to the mixture under continuous stirring. And last 90 mg of the drug was dispersed in the mixture. The solution was kept under continuous stirring on a magnetic stirrer for 30 minutes. Then the solution was poured into the petri dish and kept for 24 hours at room temperature for drying. The strip was removed from the petri dish, cut into 2x2 cm<sup>2</sup> size and preserved in aluminum foil and stored.

#### Evaluation of oral strip

##### Folding endurance

Folding endurance is determined by repeated folding of the strip at the same place till the strip breaks. The number of times the film is folded without breaking is computed as the folding endurance value (Mishra M, 2011).

##### Thickness

The thickness of strip can be measured by the micrometer screw gauge at the different strategic

locations. This is essential to ascertain uniformity in the thickness of the film as this is directly related to the accuracy of the dose in the strip (Nayak RK, 2011).

### Tensile strength

The tensile strength of the patch was evaluated by using the tensilemeter (Erection and instrumentation, Ahmedabad). It consists of two loaded cell grip. The lower one was fixed and the upper one was moving. Film strips with dimensions of 2x2 cm were fixed between these cell grips and force was gradually applied till the film broke. The tensile strength was taken directly from the dial reading in kg (Nayak RK, 2011).

### Percent elongation

The percentage elongation break was determined by noting the length just before the break point, the percentage elongation was determined from the below mentioned formula.

$$\text{Elongation percentage} = [(L1-L2)/L2] \times 100$$

Where, L1 is the final length of each strip and L2 is the initial length of each strip (Patel HA, 2010).

### Disintegration time

The six strips of 2x2 cm<sup>2</sup> put in the disintegration tester (USP) ED-2L at room temperature in tubes in the environment of water until they disintegrate and that time had been measured (Prabhakara P, 2011).

### Assay/drug content and content uniformity

A specified area of strip (2cmx2cm) was dissolved in 100ml methanol in volumetric flask and shaken continuously for 10 min. After filtration, 1 ml was withdrawn from the solution and diluted to 10ml with methanol. The absorbance of the solution was taken at 248nm and concentration was calculated which determined the drug content.

### In Vitro Drug Release test

The in vitro dissolution study of Loratadine oral strip was performed using USP apparatus (modelTDT08T,Electrolab,Mumbai,India) fitted with paddle (100rpm) at 37±0.5°C. Dissolution media were 900ml of 0.1 M HCl for 20 minutes. At the predetermined time intervals, 10ml samples were withdrawn, filtered through a 0.45µm membrane filter, diluted and assayed at 278 nm using a ShimadzuUV1800 double beam spectro-

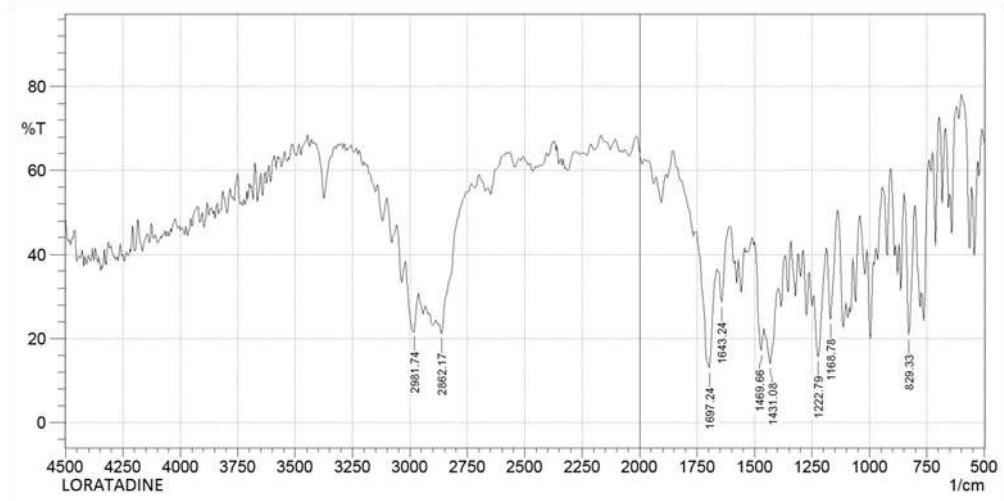


Figure 1. FT-IR spectra of pure drug.

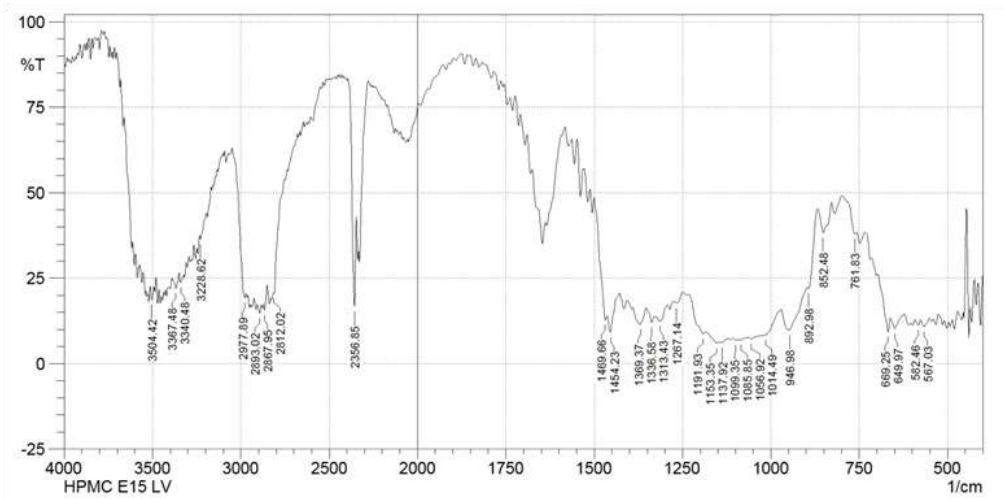


Figure 2. FT-IR spectra of polymer.

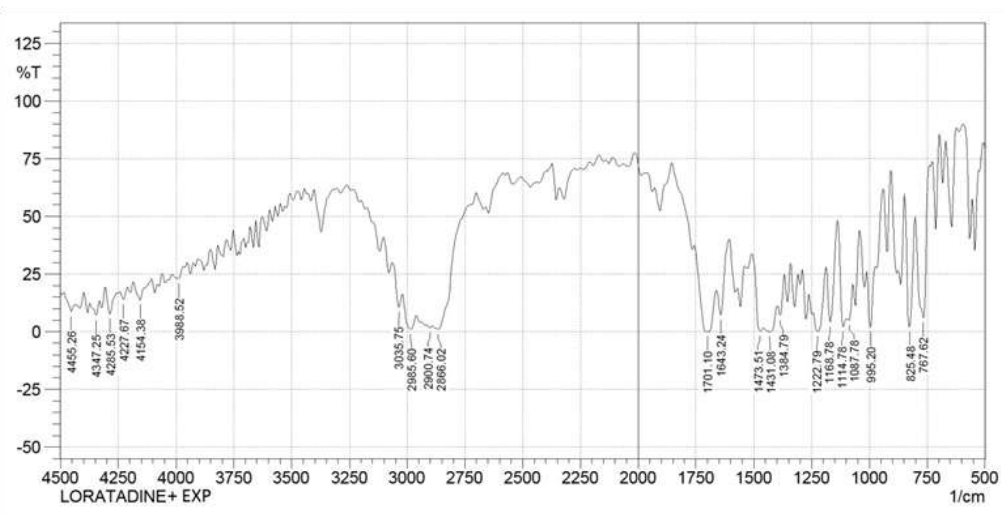


Figure 3. FT-IR spectra of composite mixture [Loratadine, HPMC E15].

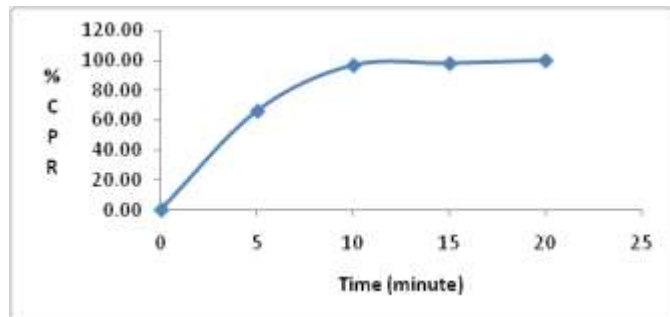


Figure 4. *In vitro* drug release study of strip.

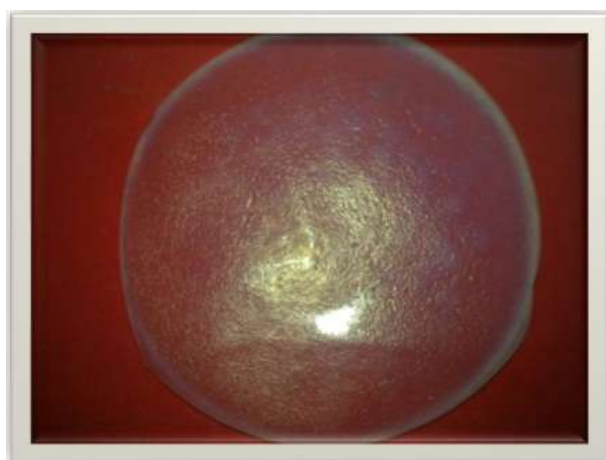


Figure 5. Photograph of oral strip.

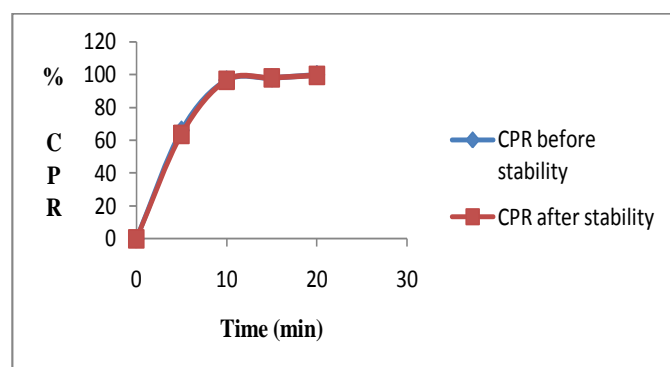


Figure 6. *In vitro* drug release study of strip before and after stability.

spectrophotometer (Shimadzu, Kyoto, Japan). Cumulative percentage drug release was calculated. A 10 ml volume of fresh and filtered dissolution medium was added to make the volume after each sample withdrawal (Suresh B, 2006).

### Drug-excipients compatibility study

Fourier transform infrared (FT-IR) technique was used to study the physical and chemical interaction between drug and excipients. FT-IR spectra of pure drug, polymer and mixture of drug and polymer were recorded using KBr mixing method on FT-IR instrument at central instrument laboratory of our institute (FTIR-1700, Shimadzu, Kyoto, Japan). FTIR spectra of analytical reports conformed that there was no interaction between drug and excipients used shown in Figure 1-3 (Trivedi S, 2010).

### Stability studies

Stability study was carried out for 30 days in aluminum packaging and kept in humidity chamber maintained at  $40 \pm 2^\circ\text{C} / 75 \pm 5\% \text{RH}$ . At the end of studies, samples were analyzed for the characterization of drug content and other parameters. (Vishvarkarma DK, 2011).

### Differential scanning calorimetry study

The DSC study of Loratadine oral strip was performed using DSC instrument (DSC-60). The DSC study carried out on pure drug, optimized oral strip before stability and on optimized oral strip after stability. The thermograph of Loratadine oral strip was obtained by Differential scanning calorimeter (DSC) on Shimadzu C-60. 2 mg of amount was taken in aluminum cell and scanned at 300C to 3000C at 40-50 ml/min nitrogen flow rate against blank DSC aluminum cell as a reference shown in Figure 7-9. (Encyclopaedia, 2012).

## RESULTS AND DISCUSSION

Strips were prepared using different grades of HPMC E5, E15 and E50 as a polymer, glycerin, tri-ethyl citrate, castor oil, propylene glycol, PEG 200, PEG 400, PEG 600 as a plasticizer and tween 80 as a surfactant. After preliminary study the final formulation contains HPMC E15, glycerine (20% of polymer) and tween 80 (15% of polymer) was introduced for formulation of oral strip of Loratadine shown in Table 1.

The four strips coded with OS1 to OS4 (2x2 cm<sup>2</sup> size) were prepared and evaluated for folding endurance, thickness, tensile strength, disintegration time, assay, content uniformity and *in vitro* dissolution. And result of all the batches were shown in Table 2.

### *In Vitro* Drug Release Study

For *in vitro* dissolution batch OS4 had given 100% drug release within 20 minutes shown in Table 3 and Figure 4. And all the physicochemical evaluation parameter are within

**Table 1.** Formulation of Loratadine oral strip.

Name of Ingredients	Quantity for 36 cm <sup>2</sup> in mg
Loratadine	90
HPMC E15	190
Aspartame	15
Glycerine	38(20%)
Tween 80	28.5(15%)
Ethanol(ml)	8
Dichloromethane(ml)	2

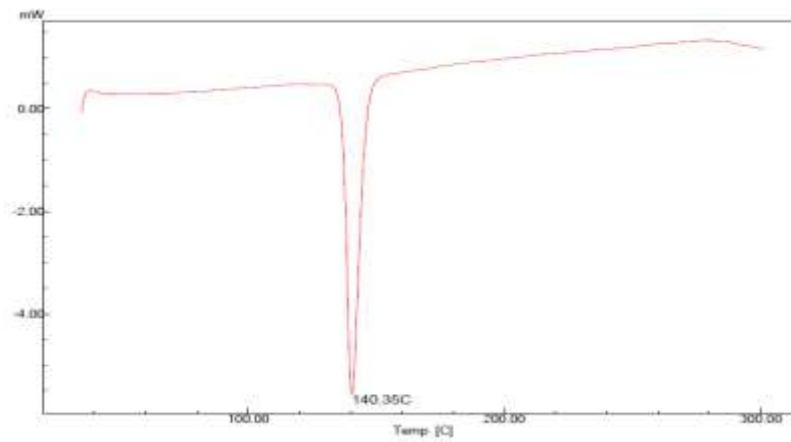
**Table 2.** Result of physicochemical parameters.

Batch code	Thickness (mm)	Tensile strength (kg/cm <sup>2</sup> )	% elongation	Folding endurance	Disintegration time (Second)	Assay (mg)	Content uniformity (mg)
OS 1	0.11	0.375	10	>400	18	9.07	9.07
OS 2	0.11	0.375	10	>400	20	9.00	9.00
OS 3	0.10	0.350	11	>400	18	9.07	9.07
OS 4	0.11	0.375	10	>400	18	9.07	9.07

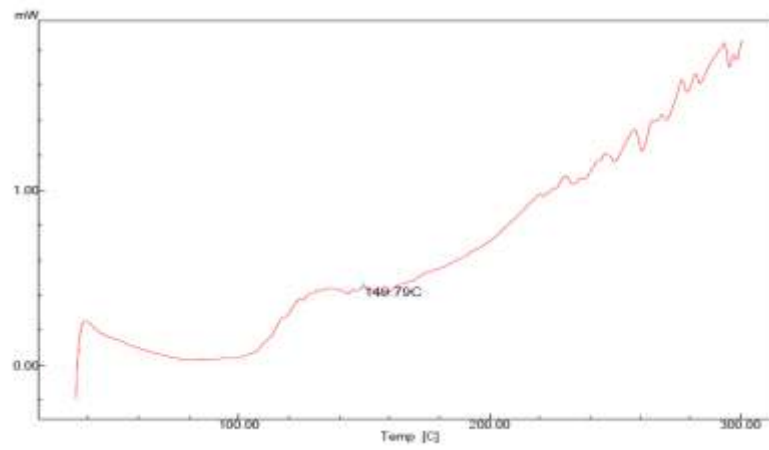
**Table 3.** Result of in vitro drug release study.

Time(min)	% CPR
0	0
5	66.15±2.37
10	96.73±0.60
15	98.07±0.04
20	99.97±0.40

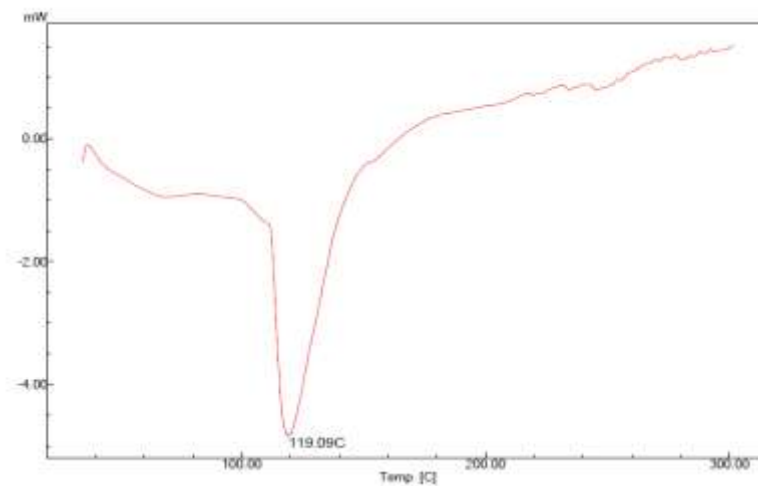
the range so, OS4 was selected as an optimized batch and photograph of oral strip is shown in Figure 5.



**Figure 7.** Thermal analysis graph of Loratadine.



**Figure 8.** Thermal analysis graph of oral strip before stability.



**Figure 9.** Thermal analysis graph of oral strip after stability.

## Stability Studies

Stability study was carried out on optimized batch for 30 days in aluminum packaging and kept in humidity chamber maintained at  $40 \pm 2$  °C /  $75 \pm 5$  % RH. Oral strip of Loratadine was found to be physically and chemically stable as they showed no significant change in terms of physical characteristics and cumulative percentage drug release shown in Figure 6.

## CONCLUSION

From the present investigation it was concluded that the amounts of polymers, plasticizers and surfactants have a significant effect on prepared oral strip. A combination of HPMC E15 LV PREMIUM and tween 80 is suitable for design of oral drug delivery system. The development of oral strip drug delivery of Loratadine strip is one of the alternative routes of administration to avoid first pass metabolism and provide immediate action. In addition, these formulations enhance patient compliance.

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