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# FORMULATION AND INVITRO EVALUATION OF LORATIDINE FAST DISSOLVING FILMS

**K. Rama Krishna***

Department of Pharmaceutics, Pulipati Prasad College of Pharmaceutical sciences,
Affiliated to Kakatiya University, Warangal, Telangana state.

***Abstract:***

*Fast dissolving films have been playing one of the important role in the current pharmaceutical research because of their convenience and ease of use over other dosage forms such as orally disintegrating tablets and immediate release tablets. In the current research, rapidly dissolving films of Loratidine were developed using low viscosity grades of HPMC and pullulan gum as film forming polymers. HPMC is a synthetic polymer which is water soluble. It is used as film former from many years. Solvent casting method is employed for the preparation of the films of Loratidine using di-chloromethane and methanol as solvents. The prepared films were evaluated for drug content, weight variation, thickness and in vitro in vivo disintegration time. Loratidine is moderately bitter drug. The taste masking was achieved by use of sweeteners and flavours. The in vitro disintegration time of the prepared formulation was found to be in the range of 18 to 50 seconds respectively. The prepared films exhibit good integrity and thickness. In vitro dissolution studies were performed as per the FDA dissolution guidelines for about 30 minutes. The optimum formulation release complete drug within 15 minutes. DSC and FTIR studies showed no drug polymer interaction.*

***Key words:*** *Fast dissolving films, HPMC, Loratidine, Solvent casting method,*

**Address for Correspondence:**
K. Rama Krishna*
Department of Pharmaceutics,
Pulipati Prasad College of Pharmaceutical sciences,
Affiliated to Kakatiya University,
Warangal, Telangana state, Pin 507 305.
Email ID:*ramakrishnakavati@gmail.com*

**INTRODUCTION**

Due to their unique properties and advantages, Fast dissolving films or rapidly dissolving dosage forms have great importance in the pharmaceutical industry [1, 2]. In less than a minute they undergo rapid disintegration in the salivary fluids of the oral cavity, where they release the drug. Most of the drug is swallowed orally with the saliva and the absorption of drug takes place in the gastro-intestinal [3.4] tract. Quick disintegrating, orally disintegrating, rapidly disintegrating, mouth dissolve or melt in mouth dosage forms are the various names referred to this fast dissolving dosage forms by researchers. [1, 3, 4]

The specific advantages for the rapidly disintegrating formulations include no water required for taking the dosage form, accuracy, immediate availability of drug at the site of absorption, rapid onset of action, ease of handling and transporting, acceptable pleasant taste and improved patient compliance. The dosage forms were first introduced in 1970's as an alternative to the conventional immediate release tablet and capsule which [3-5] require swallowing of the dosage form. The lyophilized dosage forms such as wafers, thin strips and films are sophisticated technologies for the rapidly dissolving dosage forms. These dosage forms can be manufactured using a variety of technologies, including freeze drying, vacuum drying, spray drying [1, 2] by using different super disintegrants and molding methods

Fast disintegration dosage forms are available in the market for a variety of drugs. Orally disintegrating films were introduced in the market as breath fresheners and personal care products such as dental care strips and soap strips. To achieve better therapeutic benefits these dosage forms were introduced in the United States and European pharmaceutical markets [2, 5-7]. The oral disintegrating films are prepared using water soluble and/or water swellable film forming polymer due to which the film dissolves rapidly when placed on the tongue in the oral cavity. The first oral strips were developed by the Pfizer who named it as Listerine® and were used for mouth freshening. Chloraseptic® relief strips were the first oral thin films which contained [7] benzocaine and were used for the treatment of sore throat.

At low viscosity hydroxy propyl methyl cellulose is the water soluble swellable polymer which is used as a film forming agent. The most preferred grades of HPMC film formers are HPMC E 3, HPMC E6 [8, 9]. These polymers were easily soluble in the water and gives viscous clear solution. Pullulan gum was also used in the present research work.

Loratidine is a second-generation histamine H1 receptor antagonist and derivative of azatadine which is used in the treatment of allergic rhinitis and urticaria. It lacks central nervous system depressing effects such as drowsiness. Loratidine competes with free histamine and exhibits specific, selective peripheral H1 antagonistic activity. This block the action of endogenous histamine, which subsequently leads to temporary relief of the negative symptoms brought on by histamine. Loratidine has low affinity for cholinergic receptors. In vitro it does not exhibit any appreciable alpha-adrenergic blocking activity. It also suppresses the release of histamine and leukotrienes from animal mast cells, and the leukotrienes from human lung fragments [9-18].

**MATERIALS:**

Loratidine was received as a gift sample from Strides acrolabs Banglore, India. HPMC grades were received as a gift sample from Colorcon asia PVT Ltd, Goa, India., polyethylene glycol 400 (PEG 400) were purchased from S.D. Fine Chem Ltd., Mumbai, India. Aspartame was purchased

from Himedia Lab Pvt Ltd., Mumbai, India. Banana flavor was received as gift samples from Pentagon trading company, Ahmedabad, India. All other chemicals used were of analytical grade and were used without further purification.

**METHODS:**

**Preparation of ODF:**

The FDF of Loratidine was prepared using HPMC E3, HPMC E6 and PULLULAN GUM with different ratios of 1:3, 1:6 and 1:9. The polymeric solution of HPMC was prepared by using dichloromethane and methanol in the ratio of 1:1 and kept aside for about 5 to 6 hrs for swelling of polymer shown in table-1. Loratidine was dissolved in 4 ml of dichloromethane and this drug solution was added to the above polymeric solution. This step was followed by the addition of plasticizers such as PEG 400, sweetener, flavor and color was added. Uniformity of drug content is achieved by mixing in cyclo mixer for 10 minutes. The solution was cast on a petri dish and dried at $45^0$C in hot air oven for 45 minutes. The film was carefully removed from the petri dish, then checked for imperfections and cut to the required size to deliver the equivalent dose (2.5 × 2.5 $cm^2$) per strip. Film samples with air bubbles, cuts or imperfections were excluded from the study .

**EVALUATION OF FILMS**

The weights of the films formed were determined by using electronic balance [19]. The thickness of the films was evaluated by using digital Vernier calipers [20]. The folding endurance for the prepared films was done manually. A strip of film was cut and folded repeatedly at the same place until it broke. The number of times the film could be folded at the same place without breaking is taken as the value of folding endurance [21].

**Drug content:**

Out of 5 films one film was randomly selected, weighed and added to 100ml of 0.01N HCl in a volumetric flask. The solution was sonicated for 30 mins. The solution was diluted suitably and absorbance of the resulted solution were measured using UV-Visible spectrophotometer against 0.01N HCl as blank at λ max 244 nm [20].

**In vitro disintegration time:**

Disintegration time gives an indication about the disintegration characteristics and dissolution characteristics of the film. Time required for the film to break was noted as in vitro disintegration time In vitro disintegration time of the films was determined visually in a petri glass dish with 25ml 0.01N HCl and swirling was done at every 10 sec [22].

**In vitro dissolution study: [23-25]**

In-vitro dissolution study of the prepared FDF formulations was carried out by the method suggested by USFDA dissolution methods for Loratidine. The method was USP type I (basket) by using Electro lab dissolution rate test apparatus. FDFs of desired formulation were taken and placed in the wire mesh of 700 µm and then it was placed in the vessels of dissolution apparatus. Samples were collected from the vessels at 2, 4, 6, and 10 minutes, replaced with same volume of the blank solution. The solutions were filtered through Millipore 0.45 µm syringe filter and analyzed using UV – Vis spectrophotometer. Drug concentration was calculated from the standard graph and expressed as % of drug dissolved. The release studies were performed in 6 replicates and mean values were taken.

**Fourier transforms infrared spectroscopy (FT-IR): [26]**

The FT-IR spectrum of pure drug and prepared FDF formulation were determined. FTIR (Thermo nicolet 670 spectrometer) was used for the analysis in the frequency range between 4000 and 400$cm^{-1}$ and 4$cm^{-1}$ resolution. A quality equivalent to 2 mg of pure drug was used for the study.

**Differrentential scanning colorymetry (DSC): [27]**

Thermal properties of pure drug and the formulation were evaluated by Differrentential scanning colorimetry (DSC) using a diamod (DSC) (Mettler star sw8.10).The analysis were performed at a rate $5^0$C $min^{-1}$ to 200°C temperature range under nitrogen flow of 25ml $min^{-1}$.

**RESULTS AND DISCUSSION**

Loratidine oral disintegrating films were prepared using HPMC E3, E6 and pullulan gum as film forming polymer and PEG 400 is used as plasticizer. The prepared films showed in figure-4 uniform distribution of the drug without uneven shape and air entrapments as shown in figure 2. The prepared films were evaluated for various evaluation parameters like weight variation, folding endurance, thickness, drug content etc. The results showed that all the films have a smooth surface texture. The weight variations of the films were found to be uniform within all batches. The thickness of the films was found to be in the range of 0.19 mm to 0.12 mm. The folding endurance was found to be above 300 which indicate that the plasticizer concentration was adequate. % Drug content uniformity evaluation results were found in between 98.6 ± 1.3 to 99.8 ± 1.5, thus drug was uniformly distributed in the films. The disintegration time of the films was evaluated using 0.01 N HCl buffer. The disintegration time of films in formulations F1 to F4 was in the range of 23 sec to 40 sec, in F5 to F8 it was in the range of 29 sec to 50 sec, in F9 to F12 it was in the range of 18 sec to 37sec. It was observed that the disintegrating time was increased as the concentration of polymer was increased.

**Invitro drug release study Loratidine oral disintegrating films:**

Invitro drug release of the oral disintegrating films prepared with HPMC E3, was faster at initial 5 minutes ranging from 75 to 65% in the formulation and the dissolution rate were slower as the polymer concentration was increased. However all the formulations released 99% within 30 mins. Invitro drug release of the oral disintegrating films prepared with HPMC E6, the formulation F5 showed complete drug release in 25 mins. The formulation showed only 96 to 89 % of drug release at the end of 30 mins. Invitro drug release of the films prepared with pullulan gum, the formulation F9 showed 95 % of drug release in 15 mins and complete drug release within in 20 mins. Formulation F10 to F12 extended the drug release up to 30 mins. This clearly indicated the drug release from FDF was mainly depends on the polymer viscosity and the concentration of the polymer used in the formulation. Plots for the cumulative drug released vs. time were showed in Figures1-3.

**DRUG AND EXCIPIENT COMPATIBILITY:**

**Differential Scanning Calorimetric (DSC) study:**

The prepared formulations were evaluated for DSC studies. Results of the DSC study of pure drug showed sharp endothermic peak at 134.8°C. Similar endothermic peaks were obtained in the formulations at 134.4°C clearly indicated that there was no drug polymer interaction. Results of DSC thermograms were showed in the figure 5.

**Fourier Transform Infrared Spectroscopy (FT-IR) study:**

The physicochemical compatibility between the pure drug and polymers was established through FTIR studies. The FTIR spectrum of pure Loratidine showed 1703cm−1 (C=O of ester), 1560 and 1474cm−1 (stretching vibrations of benzene ring), and 1227cm−1 (C–O stretching), similar spectrum points in the prepared formulation were

shown in the FTIR spectrum further conformed that there is no drug polymer interaction. The FTIR spectrum of pure drug and the prepared ODF were given in figure 6.

**CONCLUSION:**

The results of the present study indicated that HPMC based fast disintegrating films of Loratidine

were showed good physico chemical properties and the method solvent casting can be successfully adopted for the preparation of films. Taste masking was achieved with the use of aspartame and banana flavor. The prepared formulations were shown good mechanical properties. It was found that the polymers HPMC E3, E6 and pullulan gum has good film forming properties. The formed films were smooth in texture and have good folding endurance. The drug release was faster in the films formulated with pullulan gum than when formulated with HPMC E3, E6. The best formulation was selected from the film forming capacity and the invitro dissolution profile.

**Table 1 Formulation and physico chemical characteristics of the prepared fast disintegrating films of Loratidine**

| **Ingredients** | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** | **F7** | **F8** | **F9** | **F10** | **F11** | **F12** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Quantity in Mg** | | | | | | | | | | | |
| Loratidine | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| HPMC E3 | 200 | 400 | 600 | 800 | - | - | - | - | - | - | - | - |
| HPMC E6 | - | - | - | - | 200 | 400 | 600 | 800 | - | - | - | - |
| Pullulan gum | - | - | - | - | - | - | - | - | 200 | 400 | 600 | 800 |
| Dichloromethane (ml) | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 | 12 |
| Methanol (ml) | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 |
| PEG 400 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| Aspartame | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 |
| Banana flavor | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

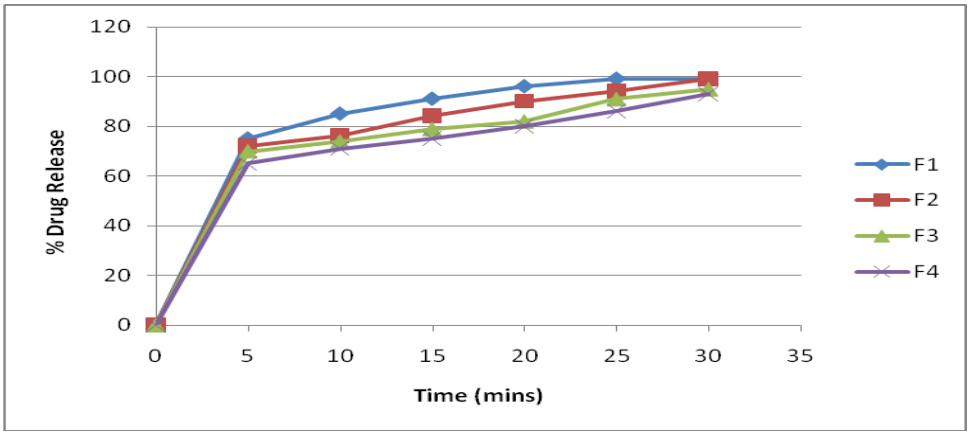


**Figure 1: Invitro drug release study Loratidine oral disintegrating films prepared with HPMC E3**

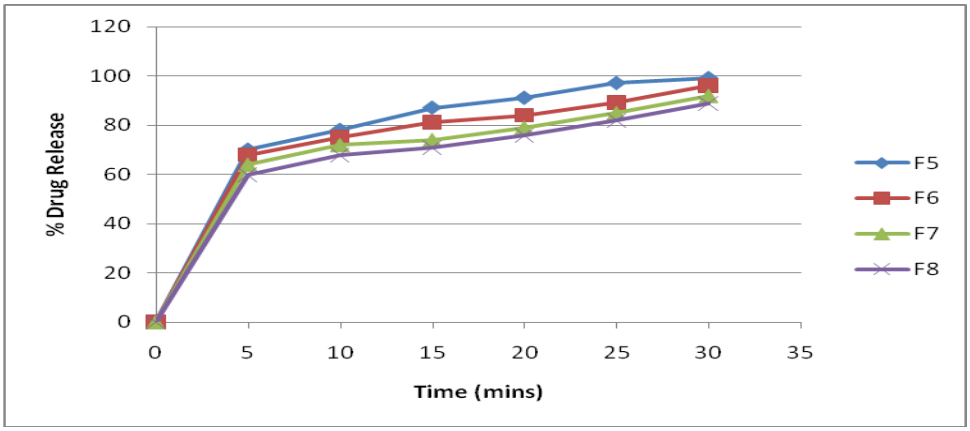


**Figure 2: Invitro drug release study Loratidine oral disintegrating films prepared with HPMC E6**

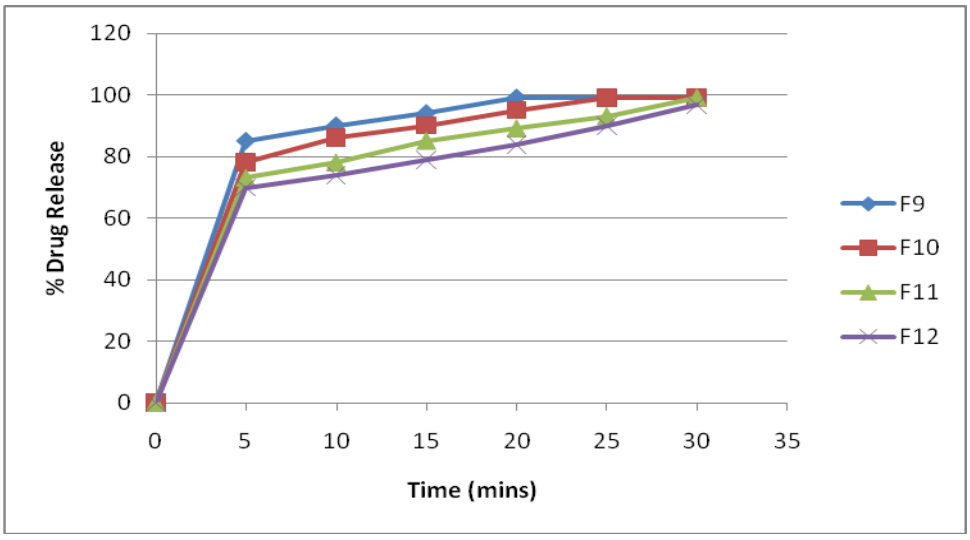


**Figure 3: Invitro drug release study Loratidine oral disintegrating films prepared with Pullulan gum**


**Figure 4: Photographs showing the prepared fast dissolving films of Loratidine.**

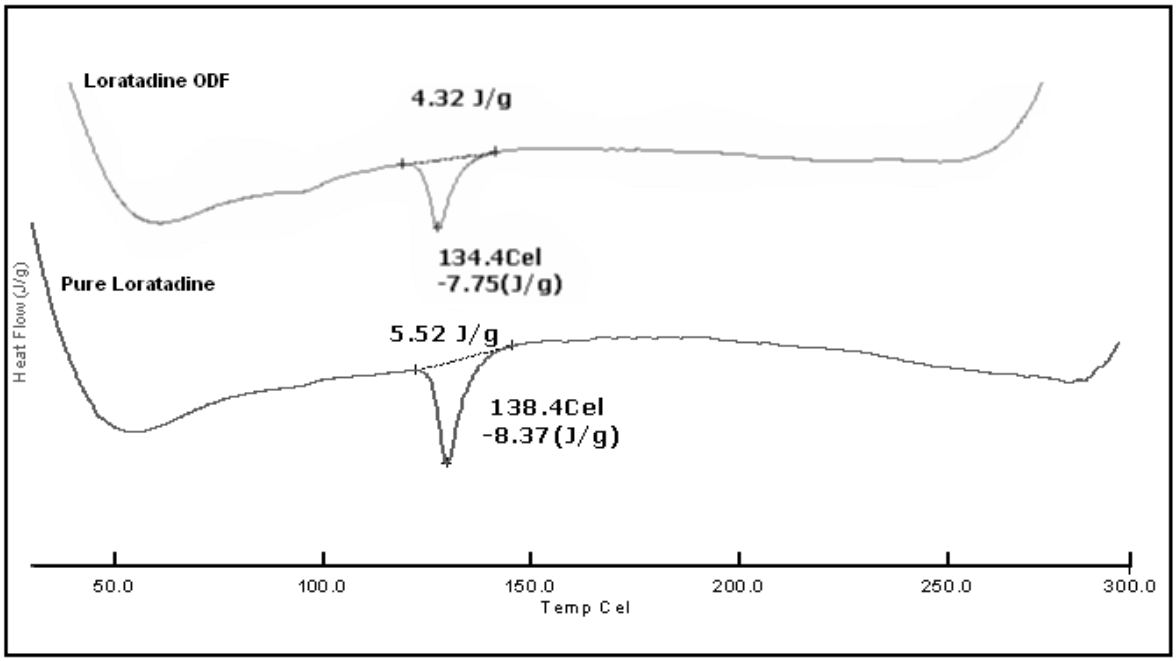


**Figure 5 DSC thermograms of pure Loratidine and Loratidine Fast disintegrating films.**

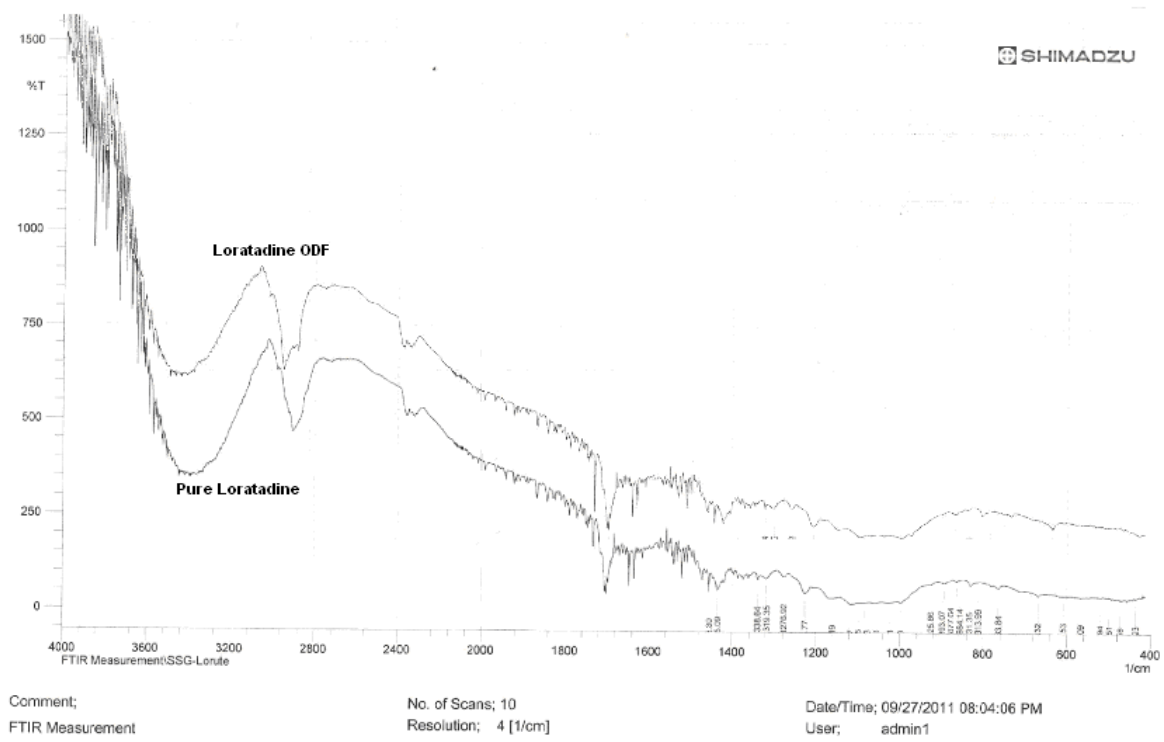


**Figure 6 FTIR Spectrum of pure drug and Loratidine Fast disintegrating films**

**REFERENCES:**

1. Liang AC, Chen LH, 2001, Fast Dissolving Intraoral Drug Delivery Systems, Exp. Opin. Ther. Patents., 11,981.

2. Borsadia S, Halloran DO, Osborne JL, 2003,. Quick Dissolving Films-A Novel Approach to Drug Delivery, Drug Delivery Technology; 3, 63.

3. Klancke J, 2003, Dissolution Testing of Orally Disintegrating Tablets, Dissolution technologies; 10, 6.

4. Parakh SR, Gothoskar AV, 2003, Review of Mouth Dissolving Tablet Technologies, Pharm Tech; 27, 92.

5. Vondrak B, Barnhart S 2008, Dissolvable films for flexible product format in drug delivery. Pharm Tech; S, 20.

6. Arnum PV. 2006, Outsourcing Solid Dosage Manufacturing, Pharm Tech. 30, 44.

7. Ghosh T, Pfister W. Drug Delivery to the Oral Cavity: Molecules to Market. Florida: CRC Press, Taylor & Francis; 2005.

8. Raymond CR, Paul J S, Sian C , , Hand book of Pharmaceutical excipients ., 4th Ed., 297; 2003.

9. Corniello CM., 2006, Drug Delivery Technology., 6, 68.

10. Chen X, Ji ZL, Chen YZ: TTD: Therapeutic Target Database. Nucleic Acids Res. 2002 Jan 1;30(1):412-5. Pubmed

11. Cieslewicz G, Gondorowicz K, Grzelewska-Rzymowska I, Rozniecki J, Wojciechowska B: [Effect of loratadine—selective antagonist of histamine (H1) receptor—on allergen-induced bronchoconstriction in atopic asthmatics] Pneumonol Alergol Pol. 1992;60(11-12):11-5. Pubmed

12. Cieslewicz G, Gondorowicz K, Grzelewska-Rzymowska I, Rozniecki J: [Effect of loratadine, selective antagonist of histamine H1 receptors, on histamine-induced bronchoconstriction] Pneumonol Alergol Pol. 1995;63(5-6):281-5. Pubmed

13. Letari O, Miozzo A, Folco G, Belloni PA, Sala A, Rovati GE, Nicosia S: Effects of loratadine on

cytosolic Ca2+ levels and leukotriene release: novel mechanisms of action independent of the anti-histamine activity. Eur J Pharmacol. 1994 Feb 15;266(3):219-27. Pubmed

14. Cavero I, Mestre M, Guillon JM, Heuillet E, Roach AG: Preclinical in vitro cardiac electrophysiology: a method of predicting arrhythmogenic potential of antihistamines in humans? Drug Saf. 1999;21 Suppl 1:19-31; discussion 81-7. Pubmed

15. Tamura T, Masaki S, Ohmori K, Karasawa A: Effect of olopatadine and other histamine H1 receptor antagonists on the skin inflammation induced by repeated topical application of oxazolone in mice. Pharmacology. 2005 Dec;75(1):45-52. Epub 2005 Jun 7. Pubmed

16. Grzelewska-Rzymowska I, Gondorowicz K, Cieslewicz G, Roznіecki J, Wojciechowska B: [Effect of loratadine (LO), a selective H1 antagonist, on histamine-induced bronchoconstriction] Pneumonol Alergol Pol. 1992;60(11-12):16-21. Pubmed

17. Menardo JL, Horak F, Danzig MR, Czarlewski W: A review of loratadine in the treatment of patients with allergic bronchial asthma. Clin Ther. 1997 Nov-Dec;19(6):1278-93; discussion 1523-4. Pubmed

18. Howarth PH: Histamine and asthma: an appraisal based on specific H1-receptor antagonism. Clin Exp Allergy. 1990 Aug;20 Suppl 2:31-41. Pubmed

19. Raghavendra Rao NG, Suryakar VB. Formulation and evaluation of Montelukast sodium mucoadhesive buccal patches for chronic asthma attacks. International Journal of Pharma and Bio Sciences 2010; 1(2): 1-14.

20. Patel R, Shardul N, Patel J, Baria A. Formulation, development & evaluation of oral fast dissolving anti-allergic film of levocetrizine dihydrochloride Arch Pharm Sci & Res 2009; 1(2):212 – 217.

21. Mahesh A, Shastri N, Sadanandam M. Development of taste masked fast disintegrating films of levocetirizine dihydrochloride for oral use. Curr Drug Deliv 2010; 7:21–7.

22. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving strips: A novel approach for the delivery of verapamil. Int J ChemTech Res 2010; 2(1).

23. Patel R, Naik S, Patel J, Baria A. Formulation development and evaluation of mouth melting film of ondansetron. Arch Pharm Sci Res 2009; 1:212–7.

24. Mohammed A, Harish N, Charyulu R, Prabhu P. Formulation of chitosan-based ciprofloxacin and diclofenac film for periodontitis therapy. Trop J Pharm Res 2009; 8:33–41.

25. Siewert M, Dressman J, Brown CK, Shah VP. FIP; AAPS. FIP/AAPS guidelines for dissolution/in vitro release testing of novel/special dosage forms. AAPS PharmSciTech 2003; 4:E7.

26. Vidyadhara S, Balakrishna T, Sasidhar RLC, Showri Babu CH, Lakshmi Harika D. Formulation and evaluation of zolmitriptan fast dissolving buccal films. Scholars Research Library Der Pharmacia Lettre 2013; 5 (4):145-152.

27. Patil A, Shaik M, Gulam I. Floating tablets of nimodipine and its inclusion complex with β-cyclodextrin for controlled release. Int J Pharm Tech Res 2011; 3(2):619-625.