The Pharma Innovation

ISSN: 2277- 7695
CODEN Code: PIHNBQ
ZDB-Number: 2663038-2
IC Journal No: 7725

ISSN 2277-7695

Received: 10-01-2013
Accepted: 23-03-2013

Vol. 2 No. 2 2013
Online Available at www.thepharmajournal.com

THE PHARMA INNOVATION - JOURNAL

Formulation and Evaluation of Fast Dissolving Films of Loratidine by Solvent Casting Method

P. Narayana. Raju[*1] , M. Sravan Kumar[1], Ch. Madhusudhan Reddy[1],and K. Ravishankar[1]

1. Department of Pharmaceutics and Industrial Pharmacy, KLR Pharmacy college, Paloncha, Khammam Dist. Andhrpradesh, India
[E-mail nrpadala@rediffmail.com]

Fast dissolving films have been played an important role in the current pharmaceutical research. They have convenience and ease of use over other dosage forms such as orally disintegrating tablets and immediate release tablets. In the present research, rapidly dissolving films of loratidine were developed using low viscosity grades of HPMC as film forming polymers. HPMC is a water soluble synthetic polymer which was used as film former form many years. The films of loratidine were prepared by solvent casting method 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, taste masking was achieved by use of sweeteners, flavours and citric acid. Type of flavor significantly affected the taste masking propderty. The in vitro and in vivo disintegration time of the optimized formulation was found to be below 29 seconds and 24 seconds respectively. The prepared films exhibited good integrity and thickness. In vitro dissolution studies were performed as per the FDA dissolution guidelines for about 10 minutes, the optimum formulation released complete drug with in 4-6 minutes. DSC and FTIR studies showed no drug polymer interaction.

Keyword: Fast Dissolving Films, Loratidine, HPMC, Solvent Casting, Taste Masking

1. Introduction

Fast dissolving films or rapidly dissolving dosage forms have great importance in the pharmaceutical industry due[1,2] to their unique properties and advantages. They undergo rapid disintegration in the salivary fluids of the oral cavity in less than a minute, 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. The fast dissolving dosage forms are referred by various names by researchers like quick disintegrating, orally disintegrating, rapidly disintegrating, mouth dissolve or melt in mouth dosage forms[1,3,4].

These rapidly disintegrating formulations having certain specific advantages like 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 newly developed 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 disintegrents 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. However these dosage forms are introduced in the United States and European pharmaceutical markets for [2,5-7] better therapeutic benefits. 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.

Hydroxy propyl methyl cellulose is the water soluble swellable polymer which was used as a film forming agents at low viscosity. The most preferred grades of HPMC film formers are HPMC E 3, HPMC E6 and HPMC E 15[8,9]. These polymers were easily soluble in the water and gives viscous clear solution.

Loratadine is used in the treatment of allergy[10,11]. Fast dissolving films of this drug gives better therapeutic benefits for the pediatric and bedridden or developmentally disabled patients. Thus, a FDF would serve as an ideal dosage form for the patients as well as paediatric patients who find it difficult to swallow the tablet. Due to its ease of usage and high acceptability, FDF of Loratadine was formulated in the present investigation.

2. Materials and methods

2.1 Materials

Loratadine 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. Orange flavour 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.

2.2 Methods

2.2.1 Preparation of ODF

The FDF of Loratadine were prepared using HPMC E3, HPMC E6 and HPMC E15 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. Loratadine 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 colour 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 450C 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.

2.2.2 Evaluation of ODF

Thickness Evaluation

The thickness of the FDF was evaluated using digital vernier calipers (Mitutoyo, Japan) The FDF sample equivalent to dose of the drug was taken and the average of three readings was taken as mean thickness. The results are shown in Table No.1 and 2.

2.3 In Vitro Disintegration Studies[2]

Disintegration time gives an indication about the disintegration characteristics and dissolution characteristics of the film. The film as per the dimensions required for dose delivery was placed on a stainless steel wire mesh placed in a petridish containing 10 ml distilled water. Time required for the film to break was noted as in vitro disintegration time in Table No.1.

Table 1: Formulation characteristics of the prepared fast disintegrating films of Loratadine

Ingredients	F1	F2	F3
	Quantity in mg		
	100	100	100
HPMC E3	300	600	900
DCM*	12	12	12
Methanol*	8	8	8
PEG 400	50	50	50
Aspartame	40	40	40
Orange flavor	10	10	10
	F4	**F5**	**F6**
Loratadine	100	100	100
HPMC E6	300	600	900
DCM*	12	12	12
Methanol*	8	8	8
PEG 400	50	50	50
Aspartame	40	40	40
Orange flavor	10	10	10
	F7	**F8**	**F9**
Loratadine	100	100	100
HPMC E15	300	600	900
DCM*	12	12	12
Methanol*	8	8	8
PEG 400	50	50	50
Aspartame	40	40	40
Orange flavor	10	10	10

* Processing solvent in the preparation of films, not present in the final formulation.

Table 2 Physico chemical characteristics of the prepared fast disintegrating films of Loratadine

Code	Thickness	Assay	DT	
	(mm)	(%)	In vitro	In vivo
F-1	0.11	98	25	20
F-2	0.12	98	29	24
F3	0.14	99	39	35
F4	0.12	99	29	23
F5	0.13	99	33	30
F6	0.14	98	46	41
F7	0.14	99	41	38
F8	0.16	99	56	50
F9	0.17	99	64	59

2.4 In Vitro Dissolution Study

In-vitro dissolution study of the prepared FDF formulations was carried out by the method suggested by USFDA [12] dissolution methods for Loratadine. 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 syrange 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.

2.5 Fourier Transform Infrared Spectroscopy (FT-IR)

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 400cm-1 and 4cm-1 resolution. A quality equivalent to 2 mg of pure drug was used for the study.

2.6 Differrentential Scanning Colorymetry(DSC)

Thermal properties of pure drug and the formulation were evaluated by Differrentential scanning colorymetry (DSC) using a diamod (DSC) (Mettler star sw8.10).The analysis were performed at a rate 50C min-1 to 200oC temperature range under nitrogen flow of 25ml min-1.

3. Results and Discussion

The Loratadine FDFs were prepared and evaluated for various physico chemical properties. The prepared formulations showed uniform distribution of the drug throughout the film. In vitro dissolution of the prepared FDFs F-1 and F-2 prepared at 1:3 and 1:6 drug polymer concentration released the complete drug in 6 minutes. As the drug is rapidly absorbed form the GI tract, the initial dissolution time points were very important. The formulation F-3 prepared

using 1:9 ratio released only 89 % of the drug in 10 minutes. In case of formulations prepared with HPMC E6, the formulations F-4 was released the completed drug in 10 minutes where as the formulation F-5 and F-6 released only 88 % and 70 % respectively with in 10 minutes. The formulation prepared with HPMC E 15 (F-7- F-9) was unable to release the complete drug with in 10 minutes due to its increased polymer viscosity. 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 Figure1.

The prepared ODF showed better film forming property due to the addition of PEG 400. The prepared films showed uniform distribution of the drug with out uneven shape and air entrapments as shown in figure 2 The thickness of all the formulation was found between 0.11 to 0.17 mm. The thickness was increased as the polymer proportion increased. In vitro and in vivo disintegration of the formulation prepared with HPMC E 6 was below 39 sec and 35 sec respectively. The taste masking of the formulations was achieved by using aspartame. In vivo taste evaluation showed better taste than the pure drug.

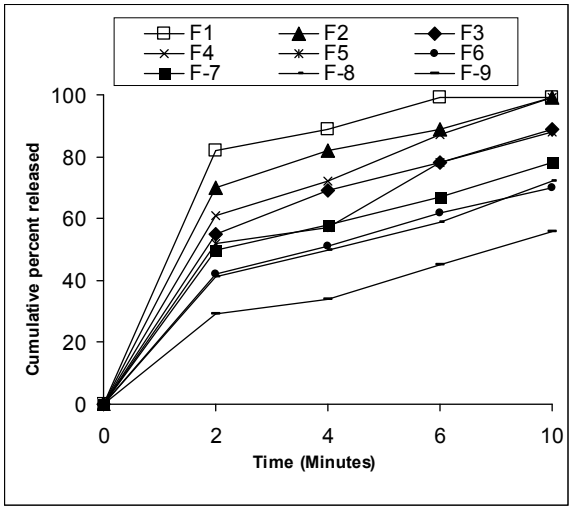

Fig 1: In Vitro Dissolution Profiles of the Prepared FDF of Loratidine

Fig 2: Photographs Showing the Prepared Fast Dissolving Films of Loratadine

The prepared formulations were evaluated for DSC and FTIR studies. Results of the DSC study of pure drug showed sharp endothermic peak at 134.8^{O}C. Similar endothermic peaks were obtained in the formulations at 134.4OC clearly indicated that there was no drug polymer interaction. Results of DSC thermograms were showen in the Figure 3.

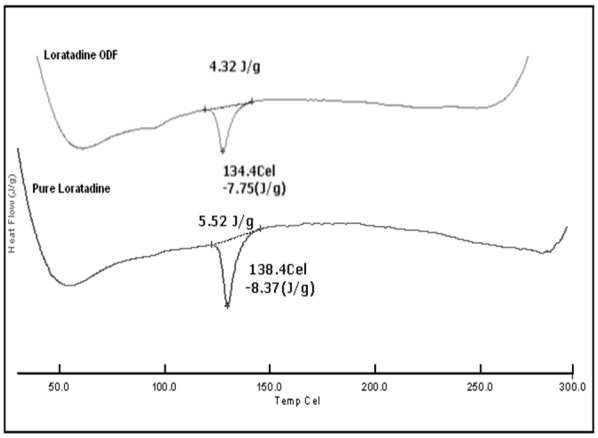

Fig 3: DSC thermograms of pure Loratadine and Loratadine Fast disintegrating films

The FTIR spectrum of pure Loratadine 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 prpepared ODF were given in Figure 4.

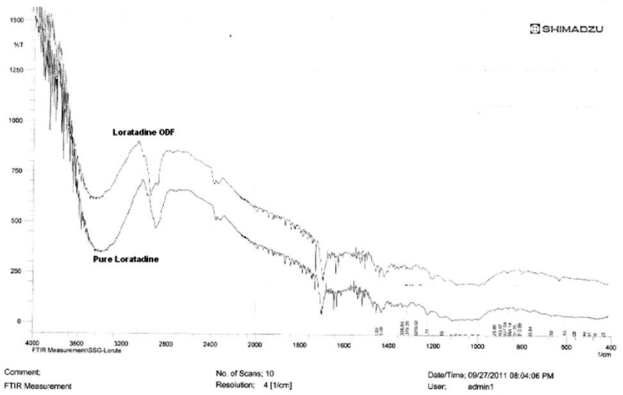

Fig4: FTIR Spectrum of Pure Drug and Loratadine Fast Disintegrating Films

4. Conclusions

The results of the present study indicated that HPMC based fast disintegrating films of loratadine 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 orange flavor. The prepared formulations were shown good mechanical properties. The films were having good commercial success.

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