



# Development and Assessment of Quick Dissolving Film of Bilastine

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## Abstract:

The aim of this research work was to develop Quick dissolving films of Bilastine, with the goal of achieving a fast onset of action to improve the management of allergic rhinitis. Using the solvent-casting method, six batches were formulated of Quick dissolving films, by using HPMC K4M, HPMC K100 as film-forming polymers. Various evaluation parameters such as thickness, weight variations, folding endurance, surface pH, disintegration, drug content, and in-vitro drug release were evaluated for all formulated batches. Among the formulated variations, F2 exhibited exceptional characteristics, lower disintegration time of only 18 seconds. Moreover, it demonstrated the highest drug release, with an impressive 95.32% of the drug being released within just 30 minutes, surpassing the performance of the other formulations. Thus, F2 was selected as the optimized formulation. Analysis through FTIR indicated that there were no significant interactions between the drug and the polymers used in the optimized formulation. In conclusion, the development of oro-dispersible film of Bilastine represents a promising approach for the treatment of allergic rhinitis. These films offer the advantage of rapid dissolution, leading to enhanced therapeutic efficacy.

**Keywords:** Mouth Dissolving Films, Bilastine, Allergic rhinitis

## Introduction:

Oral film technology was initially created in the late 1970s to address the difficulties faced by elderly and young patients who have trouble swallowing tablets and capsules. However, it has gained popularity in the pharmaceutical industry due to its numerous advantages, including increased durability, rapid release, precise dosing, and ease of administration.<sup>(1-5)</sup> The oral route of drug delivery is preferred for its cost-effectiveness and convenience, leading to high patient adherence, especially among the elderly and pediatric populations. Nevertheless, the challenge of swallowing difficulties necessitates the development of innovative and safer drug delivery systems such as oral strips and buccal films.<sup>(6-10)</sup>

Fast-dissolving films have become increasingly popular as an alternative to fast-dissolving tablets because they quickly dissolve upon contact with wet surfaces like the tongue, eliminating the need for additional liquids. This convenience not only provides a marketing advantage but also enhances patient compliance. Furthermore, the drug is directly absorbed into the systemic circulation, bypassing degradation in the gastrointestinal tract and the first-pass effect. These advantages have contributed to the widespread acceptance and popularity of this formulation, particularly among pediatric and geriatric patients and individuals with a fear of choking. Oral thin films are now approved and utilized as a technique for achieving systemic distribution of active pharmaceutical ingredients (APIs) in over-the-counter (OTC) medications and some prescription treatments.<sup>(11-14)</sup>

Fast-dissolving oral films are formulated using hydrophilic polymers that dissolve rapidly on the tongue or buccal cavity, facilitating drug delivery to the systemic circulation upon contact with liquid. The user applies the film on or under the tongue (sublingual) or along the inside of the cheek (buccal) for oral administration. These films are typically postage stamp-sized, with a similar shape and thickness. By bypassing first-pass metabolism through this drug delivery method, the medication's bioavailability is enhanced. A major challenge in developing fast-dissolving oral films lies in taste masking, as medications administered in the oral cavity should have an acceptable taste. Taste plays a crucial role in the development of oral pharmaceuticals, particularly in pediatric medicine, as it influences patient acceptance, compliance, and the market success of oral formulations regardless of the administration mode.<sup>(14-19)</sup>

**Materials:**

Bilastine is obtained from Concept Pharma Aurangabad. HPMC (K4M, K15) was obtained by Research-lab fine chemicals industries in Mumbai, along with Mannitol and Aspartame. Polyethylene glycol is sourced from Gateefoseas, a company located in Mumbai. Citric Acid is supplied by Thomas Baker Pvt. Ltd, based in Mumbai. Finally, Vanillin is sourced from Ranbaxy Fine Chemicals Limited, located in New Delhi.

**Pre-formulation Study****Characterization of Bilastine :**

**Description:** Color and physical form of Bilastine were checked visually.

**Solubility:** Solubility of Bilastine was checked in water and different pH buffers (pH 1.2, 4.5, 6.8, and 7.4).

**Melting Point:** The melting point of Bilastine was determined by introducing a small amount of the substance in a capillary attached to a graduated thermometer, and constant heat was applied with the assembly suspended in a melting point apparatus. The temperature at which the substance melted was noted.

**Spectroscopy****Determination of  $\lambda$  max of Bilastine:**

Weigh accurately 10 mg of Bilastine, transfer it into a 100 mL volumetric flask, and make up the volume to 100 mL with phosphate buffer (pH 6.8). From this solution, 1 mL was withdrawn and added to a 10 mL volumetric flask and diluted up to 10 mL with phosphate buffer (pH 6.8). Finally, the sample was scanned in the range of 200-400 nm. The wavelength of the maximum absorption was noted, and the UV spectrum was recorded.

**Standard Calibration Curve of Bilastine in Phosphate Buffer (pH 6.8):**

Accurately weigh 100 mg of Bilastine and add it to a 100 mL volumetric flask. Make up the volume to 100 mL with phosphate buffer (pH 6.8) (1000  $\mu\text{g/mL}$ ). From this solution, 10 mL was withdrawn and added into a 100 mL volumetric flask, and the volume was made up to 100 mL with phosphate buffer (pH 6.8) (100  $\mu\text{g/mL}$ ). This solution was used as the stock solution. From the stock solution, 2,4,6,8,10,12 and 14 mL of solution was withdrawn and added into a 10 mL volumetric flask and finally diluted up to 10 mL with phosphate buffer (pH 6.8). The absorbance was measured for each solution at 280 nm using a UV-Visible spectrophotometer. The graph was plotted for absorbance vs. concentration.

**Formulation of Quick dissolving films :****Dose Calculation**

The drug to be loaded in the film was determined by the dose of the drug and the drug loading in the glass plate was determined by the area of the glass plate.

**Preparation of films by solvent casting method:**

All the ingredients were weighed accordingly. The polymer was dissolved in ethanol. The drug mannitol, citric acid and vanillin were dissolved separately in ethanol. Then polymer solution added to drug solution and plasticizer (PEG-400) added then stirred for 15 minutes to produce a clear solution, which kept aside for 15 minutes to get bubble free solution. Then solutions were casted slowly with continuous flow on glass plate to prevent formation of bubbles then it kept for drying. The dried films were gently separated from glass plate and evaluated.

**Formulation design:**

Oro-dispersible oral films were prepared using various grades of HPMC as polymer.

Sr.No	Ingredients	F1	F2	F3	F4	F5	F6
1	Bilastine	20	20	20	20	20	20
2	HPMC K4M	25	30	35	-	-	-
3	HPMC K15	-	-	-	25	30	35
4	PEG 400 (ml)	0.03	0.03	0.03	0.03	0.03	0.03

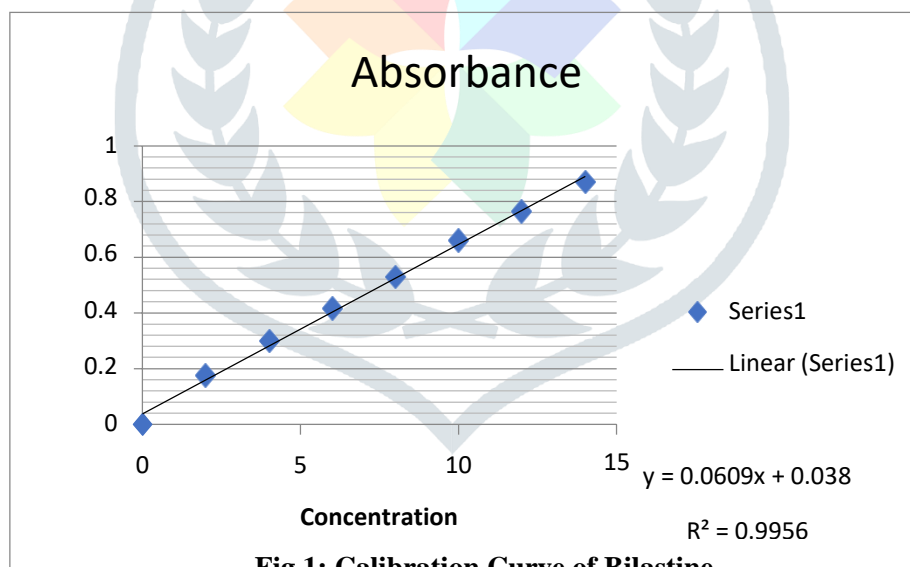
5	Aspartame	5	5	5	5	5	5
6	Mannitol	10	10	10	10	10	10
7	Citric Acid	5	5	5	5	5	5
8	Vanillin	1.5	1.5	1.5	1.5	1.5	1.5
9	Ethanol(ml)	q.s	q.s	q.s	q.s	q.s	q.s

**Results and Discussion:**

Standard calibration curve of Bilastine

Concentration	Absorbance
0	0
2	0.1758
4	0.2987
6	0.4168
8	0.5284
10	0.6594
12	0.7648
14	0.8704

**Table 1: Calibration Curve of Bilastine**



**Fig 1: Calibration Curve of Bilastine**

**Evaluation:**

Formulation Batch	Appearance	Tack Test	Film Thickness(mm)	Tensile Strength (Kg/mm)

F1	Transparent	Non Tacky	0.7±0.04	0.216±0.004
F2	Transparent	Tacky	0.9±0.10	0.220±0.002
F3	Transparent	Non Tacky	1.3±0.21	0.221±0.006
F4	Transparent	Non Tacky	0.7±0.10	0.410±0.002
F5	Transparent	Tacky	1.0±0.06	0.416±0.002
F6	Transparent	Non Tacky	1.1±0.24	0.421±0.004

**Table 2: Evaluation of Films for, Appearance Tack test, Thickness and Tensile Strength**

#### Physical Appearance and Surface Texture of Quick dissolving films :

These parameters were checked simply with visual inspection of Oro-dispersible film and by feelor touch. The observation suggests that Quick dissolving films are having smooth surface and theyare elegant enough to see.

#### Tack Test

All Strips were evaluated for tack test out of that only F2 and F5 batches were found to be tacky and other batches were found to be non-tacky The tack test of all Oro-dispersible oral filmsis given in above table.

#### Tensile Strength:

Tensile strength was found to increase with increase in concentration of the polymers. Tensile strength range of the films varied from to 0.216 ± 0.004 to 0.516±0.002 for HPMC films.

#### Thickness of Quick dissolving films :

The thickness of Quick dissolving films were measured using screw gauge and the average thickness of Oro-dispersible film given in above Table The thickness of Oro-dispersible film prepared with HPMC K4, K15, respectively.

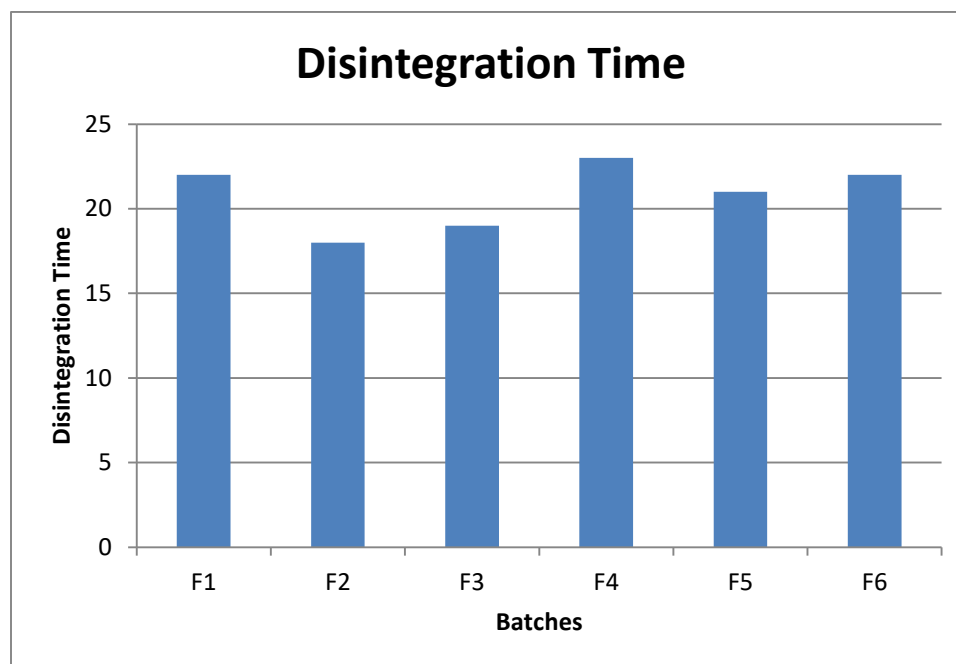
Thickness of Quick dissolving films was found between 0.7±0.04 to 1.3±0.25.

Batch	Disintegration Time (sec)	Folding Endurance	% Drug Content	Weight Variation (mg)	pH
F1	22.6 ±0.24	77 ±0.24	95.43±0.38	4.5±0.09	6.36
F2	18.3 ±0.26	90 ±0.38	98.47±0.27	6.7±0.08	6.61
F3	19.3 ±0.64	80 ±0.51	89.12±0.28	7.9±0.21	6.83
F4	23.23 ±0.12	86 ±0.24	96.54±0.98	5.5±0.11	6.81
F5	21.01 ±0.37	82 ±0.45	92.12±0.44	7.1±0.24	6.68
F6	22.77 ±0.39	81 ±0.54	90.25±0.16	6.5±0.42	6.90

**Table 3: Evaluation parameter of formulation batches.**

#### Disintegration Time of Oro-dispersible film:

Strip of 2 x 2 cm<sup>2</sup> size taken and disintegration time checked visually. In each case three Quick dissolving films were used and the average drug content was calculated, the results were shown in above table.

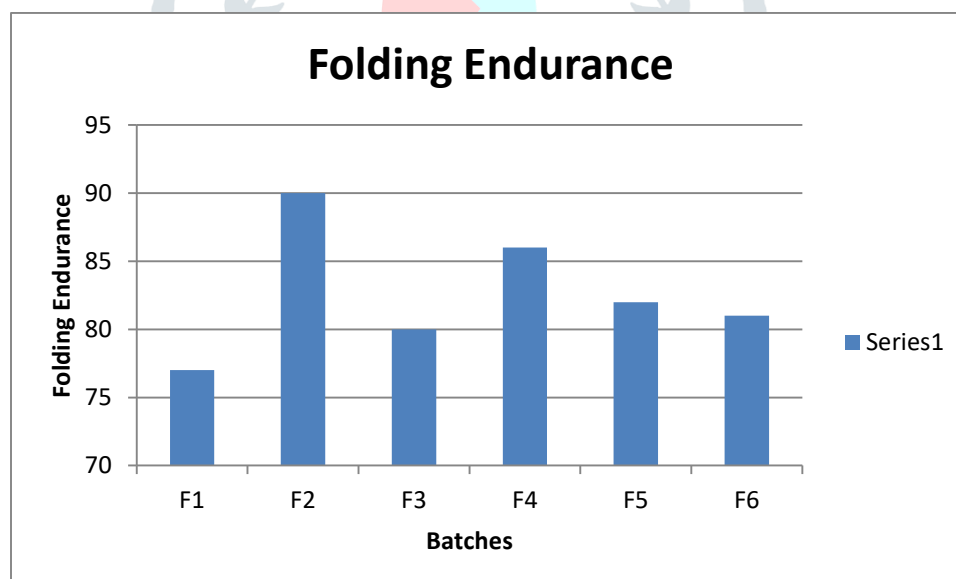


**Fig 3: Disintegration Time Prepared Films**

Disintegration times of Quick dissolving films were found between  $18.3 \pm 26$  to  $23.23 \pm 0.12$ .

#### Folding Endurance of Quick dissolving films :

The folding endurance of Oro-dispersible film was determined by repeatedly folding a small film of Oro-dispersible film at same place till it broke and the average folding endurance of all Films given in Table which ranges between in table sin between range  $74 \pm 0.24$  to  $82 \pm 54$ .



**Fig 4 : Folding Endurance Of Prepared Films**

#### Drug Content Uniformity of Quick dissolving films :

In each case three Quick dissolving films were used and the average drug content was calculated, the results were shown in above table. The drug was dispersed in the range of  $89.12 \pm 0.14$  to  $98.47 \pm 0.12$ . Suggesting that drug was uniformly dispersed in Quick dissolving films. The S.D. value calculated for such formulation is very less which suggest that the results are reproducible and accuracy in the method used to prepare Quick dissolving films.

### Weight Variation of Quick dissolving films:

Weight of Quick dissolving films was determined using digital balance and the average weights of Quick dissolving films were given in above table. The weight variation of formulated films in between  $4.5 \pm 0.09$  to  $7.9 \pm 0.57$ .

### Surface pH of Quick dissolving films:

The surface pH was noted by pH meter near the surface of Oro-dispersible film and allowing to equilibrate for 1 min and the surface pH of Quick dissolving films was given in above table the surface pH of Oro-dispersible film was found to be in-between 6.36 to 6.81 pH (n=3).

### In-Vitro Dissolution Studies of Bilastine:

Time	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	22.64	25.98	20.35	23.98	21.55	20.25
10	39.71	45.24	34.58	39.32	34.25	32.32
15	55.47	68.87	59.37	55.74	53.35	51.25
20	72.24	89.68	85.87	84.93	83.25	78.35
25	82.98	97.26	90.29	87.16	85.32	84.35
30	92.46	98.58	95.24	96.32	91.25	93.35

Table 4 : In-Vitro Dissolution studies of Bilastine

All values expressed as mean  $\pm$ SD (n=3), F=Formulation batch

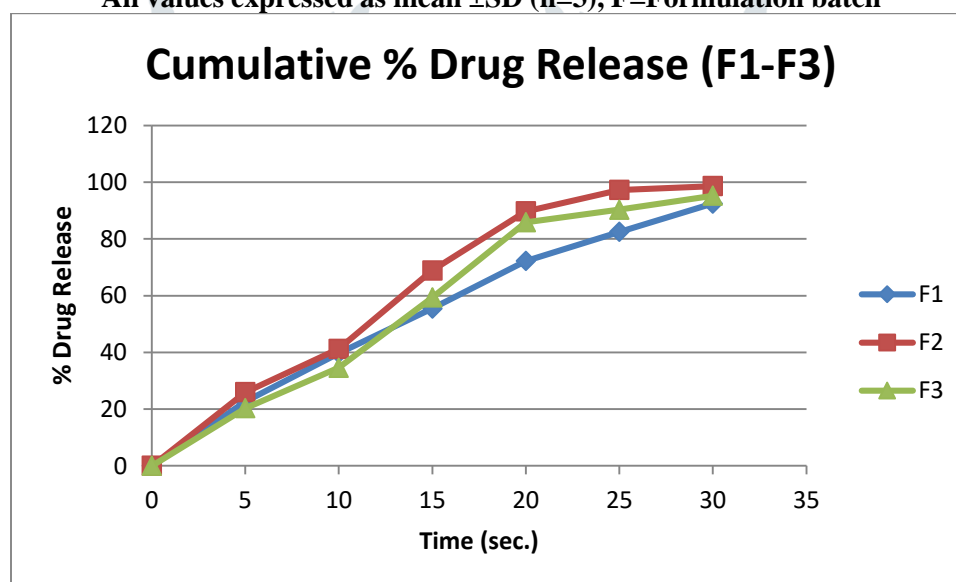
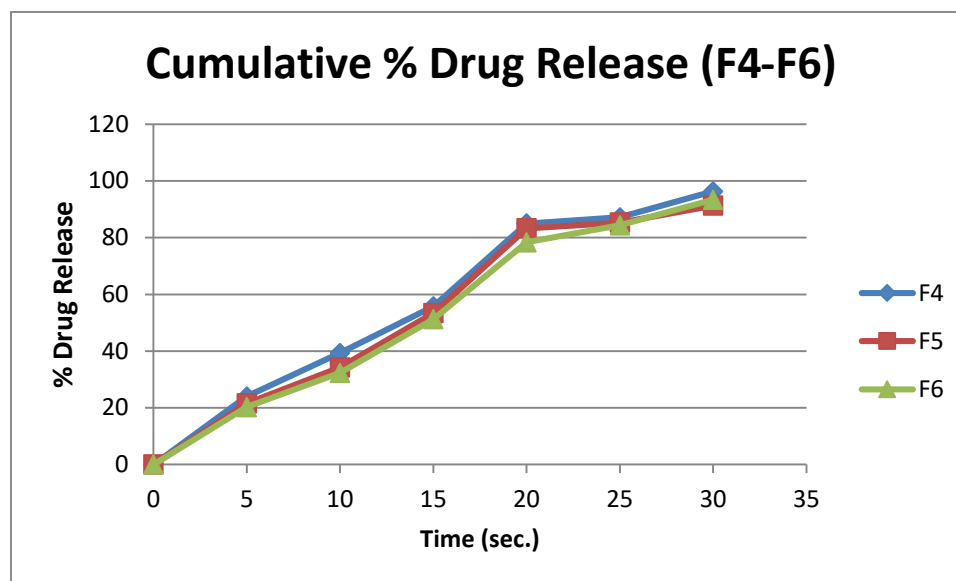


Fig 5: Cumulative % Drug Release From F1-F3



**Fig 6: Cumulative % Drug Release From F4-F6**

In these all aspects the formulation F2 satisfied all the pharmaceutical parameters of mouth dissolving films, and appears to give better therapeutic effects, with disintegration time  $18.23 \pm 0.12$  seconds 98.58 % drug release.

### Stability Studies

Stability studies for the optimized formulation (F4) was carried out in order to determine the physical stability of the formulation. The results were shown in there was no significant change in the parameters which are evaluated during the study period in the accelerated conditions

Evaluation Parameters	0 Days	30 Days	60 Days
Thickness	0.9	0.9	0.9
Weight Variation	0.79	0.79	0.76
Folding Endurance	14.24	14.24	13.51
Surface pH	6.8	6.7	6.7
Disintegration Time (Sec)	17.23	16.57	16.21
% Drug Content	96.54	96.45	96.31
Visual Inspection	Transparent	Transparent	Transparent
% Drug Release	$98.58 \pm 0.21$	$96.11 \pm 0.47$	$91.84 \pm 0.24$

**Table 10: Parameters studies on F2 formulation before and after stability study**

There were no considerable changes in physical parameter of film such as Thickness, Weight variation, Folding endurance, Disintegration time, % Drug content of formulation F2 before and after accelerated stability study.

### Summary

Bilastine is the drugs used in allergic rhinitis which is very common. The absolute bioavailability of Bilastine is approximately 61%. To overcome the above-mentioned problems an attempt was made to develop and to improve the solubility of drug and reduce side effects, it was attempted to develop Quick dissolving films using different film forming polymers. FTIR spectroscopic studies were carried out in order to establish compatibility between drug and excipients. The results were concluded that there were no chemical interactions between drug and the excipients used, so they could be used for the formulation of Quick dissolving films .

Total 9 formulations of mouth dissolving films were developed using various excipients which were found to be compatible using FTIR of films. Formulations were prepared using three different polymers such as HPMC K4M, HPMC K15.



Films were evaluated for quality control tests such as Appearance, Tack test, Thickness, Tensile strength, disintegration time, folding endurance, % Drug content, Weight variation, in-vitro dissolution, Comparison with marketed product and stability study.

The thickness of formulations was between  $0.7 \pm 0.04$  to  $1.3 \pm 0.21$ . Tensile Strength of all 9 formulations was found to be in between  $0.0216 \pm 0.004$  to  $0.516 \pm 0.002$ . The Disintegration time of the formulations was found to be between  $18.23 \pm 0.12$  to  $34.78 \pm 0.97$ .

The surface pH of all formulations was found to be in between 6.36 to 6.81. The Folding endurance of the formulations was found to be in between  $77 \pm 0.26$  to  $90 \pm 0.54$ . The % drug content of all the formulations was found to be in between  $90.25 \pm 0.28$  to  $98.47 \pm 0.27$ . The Weight variation of the formulations was found to be in between  $4.5 \pm 0.09$  to  $7.9 \pm 0.57$ .

In these all aspects the formulation Batch F2 satisfied all the pharmaceutical parameters of mouth dissolving films. So, the F2 batch was selected as optimized batch.

## Conclusion

Overall, this study successfully developed Quick dissolving films for Bilastine, which showed desirable physical characteristics and drug content. The findings suggest that the formulation approach using these film-forming polymers can be a promising strategy to enhance the solubility and minimize side effects of the drug in the treatment of allergic rhinitis. Further investigations, including in vivo studies and clinical trials, may be warranted to assess the efficacy and safety of these formulations for potential therapeutic applications.

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