ORIGINAL ARTICLE

Stability study of oral strip for anti-allergic film olopatadine hydrochloride

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Abstract

Objective: The aim of the present work was to develop and evaluate the fast-dissolving oral films (FDF) of olopatadine hydrochloride which is used for the treatment of anti-allergic. This study was to perform evaluation study of film stability, their stability of oral strip in different temperature for the easy to transport in different areas that they are not damage for the temperature conditions. **Materials and Methods:** The olopatadine hydrochloride film was prepared by solvent-casting method which is used for prepared oral strip such as hydroxypropyl methylcellulose (HPMC), maltodextrin, and polyethylene glycol, as plasticizers different polymers are used. **Results:** The prepared oral strip showed satisfactory results for the evaluation parameters oral strip as optimized batch was evaluated for stability of film in different temperatures that are used as an *in vitro* test for the evaluation of film for storage in different temperatures and their transportation stability. Olopatadine hydrochloride FDF was developed and evaluated for weight uniformity *in vitro* dispersion time, *in vitro* dissolution time, drug content, and film thickness that the results obtained were within the specified limits. Temperature stability test is used for high temperature evaluated in hot air oven, and low temperature evaluated in refrigerator. **Conclusion:** The FDF prepared with HPMC E-15, at 2, 4, 6, and 8 ratio released the drug up to 98.7% within 2 s which evaluated that their stability study in different temperatures which are evaluated showed that their stability studies were conducted for pure drug, polymers, and optimized formulation f6 which indicated that found between the drug and polymers used in the present studies evaluated that the film is stable in different temperature, polymers, and optimized formulation F6 which showed that they were no surface fractures and cracks in the films.

Key words: Film, gastrointestinal tract, hydroxypropyl methylcellulose, maltodextrin, oral strip, stability, tablet, the fast-dissolving oral films

INTRODUCTION

Oral route is most preferred route by medical practitioners and manufacturer due to highest acceptability of patients. About 60% of all dosages available are the oral' solid dosage form. The lower bioavailability, long on set time, and dysphagia (difficulty in swallowing) patient turned the manufacturer to the parenteral and liquid orals. However, the liquid oral (syrup. suspension, emulsion, and parenteral) is painful drug delivery so patient incompliance. Fast dissolving film (FDF) are a sort of solid dosage form that was developed based on the technology of transdermal patches for medication delivery through the oral route.[1,2] This delivery device consists of a thin film that is simply applied on the patient's tongue or mucosal tissue and quickly dissolves when wet by saliva. The medicine is then rapidly disintegrated and dissolved for oral mucosal absorption.[3-5] The huge surface area of the film, which wets quickly when exposed to the moisture environment, contributes to the fast-dissolving activity. FDF is made with a hydrophilic polymer that dissolves quickly on the tongue or in the buccal cavity, allowing the medicine to enter the systemic circulation through the buccal mucosa.[6] For the increase of bioavailability, quick-dissolving drug delivery systems are specifically designed for medicines with substantial first-pass metabolism. This technology evolved over the past few years from the confection and oral care businesses, becoming a novel and well-accepted form by consumers. These films have the ability to administer the medication systemically through intra-gastric, sublingual, or buccal routes of administration, as well as for local action.[7-9] In the present studies, olopatadine hydrochloride film is taken as a drug candidate for the

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development of FDF which was prepared using hydroxyl propyl cellulose, PVA, hydroxypropyle methylecellulose (HPMC) E5 as film-forming agents, and they were prepared by solvent-casting method, the film was evaluated in different temperature to check stability of film for different areas that are transported this formulation easy to store.[10]

MATERIALS AND METHODS

Olopatadine hydrochloride is a sample from drug olopatadine (Sun pharmaceutical industries Ltd.) from Sarvepalli radhakrishnan University Bhopal. HPMC-15 Oxford laboratory Mumbai, Maltodextrin (MD) (DE-20) Hamidia laboratory Pvt. Ltd., Mumbai, Propylene glycol Loba Chemical Pvt. Ltd., Mumbai.

Material

Preparation of olopatadine hydrochloride oral film

- HPMCE-15 and MD were dissolved in 10 ml water kept aside for sometime and the solution was mixed with hand stirring at 20–22 min [Figure 1 and Table 1]
- The solution was added propylene glycol and stirrer. The compositions of prepared films are given in Table 2
- The solution was kept aside for bubbles free solutions at overnight
- This solution again stirring with magnetic stirrer at 60°C for 15 min and their solution was kept aside for few minutes for bubbles kept out [Table 3]
- The drug was added in methanol and stirring then added the solutions
- The mixture was kept aside for removal of air and then casted the mixture on a glass slide and dried at hot air oven at 65°C for 30–32 min
- After drying film was removed from slide and cut in desire sizes.

The compositions of prepared films are given in Table 2.

Table 1: Polymers dissolve in water

Dispersing Time	Room temperature	Removal time of air bubbles
HPMC 22 min	38°C	22 h
Maltodextrin 11 min	38°C	12 min

Table 2: Composition of drug loaded film

Ingredients	Uses	Quantity
Olopatadine Hcl	Drug	20 mg
HPMC E-15	Polymer	2 g, 4 g, 6 g, and 8 g
Maltodextrin	Polymer	3 g, 5 g, 9 g
Propylene glycol	Plasticizer	1.35ml
Glycerin	Plasticizer	Q.S

Observation table

HPMC Polymer are dissolve in water they are disperse in 22 min in room temperature are 38◦c and their air bubble remove in 22hour and Maltodextrin polymer are dissolve in water they are disperse in 11 min in room temperature are 38◦c and their air bubble are remove in 12 min shown in Table 1 and fig show in Figure 1.

Evaluation of fast-dissolving film (FDF)

The FDFs of Olopatadine HCL were evaluated for the following properties-

Physical appearance and surface texture

This parameter was checked simply with visual inspection of film and evaluation of texture by feel and touch [Figure 2].[4]

Physical uniformity of film

Mouth dissolving film of size 2 cm × 2 cm was uniform surface of film.[9]

Thickness of films

Thickness of film was measured using screw gauge with a least count of 0.01 mm at different spot of film. The thickness was measured at three different spots of the film and average was taken [Figure 3].[10]

Surfaceph of film

Surface pH was determined by the film that was allowed in contact with 1 ml of distilled water. The surface pH 6.8 was noted by bringing glass electrode of pH paper near the surface of film and allowing equilibrates for 1 min.

Table 3: List of instrument and equipment

Name	Manufacturers
Melting point apparatus	Jyoti Scientific Industries, Gwalior
Digital weighing balance	Jyoti Scientific Industries, Gwalior

Table 4: List of chemical and solvent

Name	Supplier/Manufacturer
Olopatadine HCL	Drug from SRK university Bhopal (sun pharmaceutical industries Ltd.)
Hydroxypropyl methylcellulose (HPMC-15)	Oxford laboratory Mumbai
Maltodextrin (DE-20)	Hamidia Laboratory Pvt. Ltd., Mumbai
Propylene Glycol	Loba Chemical Pvt. Ltd., Mumbai
Glycerin	Sarafine chemical, Mumbai

Figure 1: Solution of maltodextrin and hydroxypropyle methylecellulose

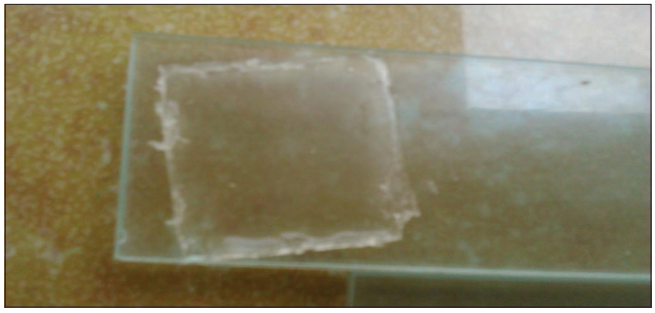


Figure 2: Anti-allergies film fast-dissolving of olopatadine HCL

Figure 3: Screw gauge micrometer

Figure 4: Fast-dissolving film

Figure 5: For high temperature used in hot air oven

Dryness test

Dryness test or the tackiness test. The aim of this test it to evaluate the tenacity of the film being able to grip the solvent and also to see the adherence of the film as it is done with eight stages known for film drying and these are set to touch, free from dusts, surface dry, dry to react, dry handling, dry to touch, dry hard, and free from finger print so dry print free.[11] Tack is defined as the persistence, in which the strip stick to a piece of paper which is pressed into contact with the strip [Figure 4].

In vitro dissolution time

Disintegration test was performed by film size required for dose delivery (2 cm × 2 cm) that was placed on a glass Petri dish containing 10 ml of distilled water the time required for the film to break which was noted as *in vitro* dissolution 3–5 s.[11]

In vitro dispersion time

The test was performed using the method the film (2 cm × 2 cm) that was placed on a glass Petri dish containing 10 ml of distilled water and gently stirred after every 1 s, the disintegration time is the time when a film starts to break or disintegrate. The time for complete dissolution of the film was recorded in triplicate as dispersion time at which no visible film part was seen and the film completely disperses in the medium.[11]

RESULTS AND DISCUSSION

Based on the physiochemical and biopharmaceutical properties, the aim of the present study was to prepare FDF of olopatadine hydrochloride using the solvent-casting method, which should possess a suitable approach in enhancing the disintegration and dissolution characteristics in more faster with increased bioavailability. Hydroxypropyl methylcellulose, polyethylene glycol, and HPMC E15 were chosen as the film-forming agents. The olopatadine hydrochloride FDF formulations were prepared by different ratios of drug and film-forming agents by solvent-casting method. The composition of olopatadine hydrochloride FDF formulations is shown in Table 4.

Evaluation of physical parameters for olopatadine hydrochloride FDF

Stability studies

The stability study of the formulated fast-dissolving films was carried out under different environmental conditions. The film was packed in the aluminum foil and stored in a stability chamber for stability studies at 2–8°C (45% RH), 25–30°C (60% RH), and 45–50°C (75% RH) for a period of 14 days. The film was characterized for the drug content and other parameters during the stability study period. Mouth dissolving film is store in high temperature 45–50°C and less then −15°C temperature. This film is stored in above 50°C temperature

S.NO	Day's	Film's Stability in different temprature °c						
		F1	F2	F3	F4	F5	F6	F7
1	1	27	30	35	40	45	50	55
2	2	27	30	35	40	45	50	0
3	3	27	30	35	40	45	50	
4	4	27	30	35	40	45	50	
5	5	27	30	35	40	45	50	
6	6	27	30	35	40	45	50	
7	7	27	30	35	40	45	50	
8	8	27	30	35	40	45	50	
9	9	27	30	35	40	45	50	
10	10	27	30	35	40	45	50	
11	11	27	30	35	40	45	50	
12	12	27	30	35	40	45	50	
13	13	27	30	35	40	45	50	
14	14	27	30	35	40	45	50	

Chart 1: Physical property and stability of room temperature to above 55°C

S.NO		cumulative % of drug released					
	Time (sec)	F1	F2	F3	F4	F5	F6
1	0.5	40	37	39	40	35	35
2	1	60	57	55	48	46	48
3	1.5	77	72	70	75	65	60
4	2	88	81	79	89	78	72
5	2.5	98	94	92	92	88	80
6	3	100	98	96	96	94	92
7	6	100	100	98	97	96	95
8	9	100	100	99	98	99	98
9	12	100	100	100	100	100	100

Chart 2: Film stability study of drug release in different room temperature to 27°C to 50°C

S.NO		Physical Property stability in different temperature						
	Time (sec)	F1	F2	F3	F4	F5	F6	F7
1	1	-5	-10	-15	-20	-25	-30	-35
2	0.25	-5	-10	-15	-20	-25	-30	0
3	4	-5	-10	-15	-20	-25	-30	
4	6	-5	-10	-15	-20	-25	-30	
5	8	-5	-10	-15	-20	-25	-30	
6	10	-5	-10	-15	-20	-25	-30	
7	12	-5	-10	-15	-20	-25	-30	
8	14	-5	-10	-15	-20	-25	-30	

Chart 3: Physical property of temperature −5°C–−35°C

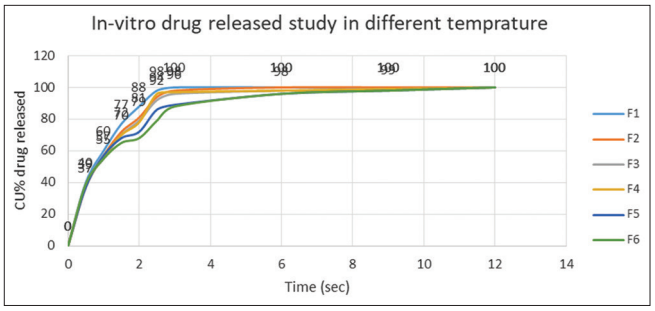
S.NO	Time (sec)	cumulative % of drug released					
		F1	F2	F3	F4	F5	F6
1	0	0	0	0	0	0	0
2	0.5	40	37	39	38	37	39
3	1	60	57	55	56	57	55
4	1.5	77	72	70	70	68	65
5	2	88	81	79	78	72	68
6	2.5	98	94	92	96	86	79
7	3	100	98	96	97	89	88
8	6	100	100	98	98	96	96
9	9	100	100	99	98.9	98	98
10	12	100	100	100	100	100	100

Chart 4: Film stability study of drug release in different −5°C–−30°C temperature

film physical property which is melted and more than 55°C film shown in [Charts 1-4], its physical property is melted and its not working [Figure 5].[5]

This chart was shown their stability in different batches film physical property in 27–55°C.

This film are stored in above −15°C temperature film its physical property, which are few hard and more then −35°C film its physical property too hard and its not working.



Graph 1: Graph of film stability study of drug release in different −5°C to temperature

This chart was shown the film stability physical property of film in different temperature −5–−35°C.

This graph was shown their drug released study in different temperature [Graph 1]. The chart was shown their stability study of drug release in different −5–−30°C temperature [Chart 4].

Packaging of FDF

In the pharmaceutical industry, it is vital that the package selected adequately preserve the integrity of the product. Expensive packaging, specific processing, and special care are required during manufacturing and storage to protect the dosage of other fast-dissolving dosage forms. A variety of packaging options are available for oral strip. Single packaging is mandatory for films, which are pharmaceutical products; An aluminum pouch is the most commonly used packaging format. Labtec has developed the Rapid card, a proprietary, and patented packaging system, which is specially designed for the Rapid films. The rapid card has same size as a credit card and holds three raid films on each side. Every dose can be taken out individually.[11]

- Packaging of oral strip of Olopatadine Hclare packet in aluminum foil and store in cool temperature mouth dissolving film are store in high temperature 45–50°C and less then −15°C temperature
- The stability study of the formulated fast-dissolving films was carried out under different environmental conditions. The film was packed in the aluminum foil and stored in a stability chamber for stability studies at 2–8°C (45% RH), 25–30°C (60% RH), and 45–50°C (75% RH) for 14 days. The film were characterized for the drug content and other parameters during the stability study period. Mouth dissolving film is store in high temperature 45–50°C and less then −15°C temperature
- This film is stored in above 50°C temperature film physical property are melted and more than 55°C film its physical property are melted and its not working.

CONCLUSION

In the present work, FDF of olopatadine Hcl were prepared by solvent-casting method using HPMC E-15, MD as a

polymer. The olopatadine Hcl is insoluble in water and its bioavailability is limited, and hence, this method is useful for improving its bioavailability of the drug. The dissolution time of film was reduced by use of MD with HPMC E-15 as a combination. Short-term stability studies of promising formulation indicated that there is no significant change in drug content and *in vitro* dissolution time. This study was evaluated their stability of film in different temperature for the benefit for easy to store in different temperature in different areas.

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