

# Formulation and Evaluation of Orally Disintegrating Films of Levocetirizine Dihydrochloride

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## Kathpalia and Patil: Formulation and Evaluation of Levocetirizine Dihydrochloride

The present investigation was undertaken with the objective of formulating taste-masked orally-disintegrating films of the bitter levocetirizine dihydrochloride to enhance the convenience and compliance by the elderly or paediatric or bedridden and non-cooperative patients due to its ease of administration. Scope of this study was to explore the film forming properties of various film formers like modified starch, pullulan, hydroxypropyl methylcellulose and polyvinyl alcohol-polyethylene glycol based polymers. Plasticizers like glycerin, propylene glycol, sorbitol and polyethylene glycol 400 were evaluated by studying their effect on folding endurance, peelability and *in vitro* disintegration time. Films were prepared by solvent casting method. Drug-loaded films, which composed of the selected polymers with the suitable plasticizer showed excellent film forming capacity along with good folding endurance, *in vitro* disintegration time within 22 s and >95% drug release in 10 min as compared to marketed immediate release tablets, which showed on 30.4% at the end of 10 min. The films prepared were 30-40 mg in weight with pleasant taste with bitter active being successfully taste masked by a mixture of sucralose and monoammonium glycerrhizinate producing an extended sweetness profile. Furthermore, the orally disintegrating films were stable for at least 3 mon when stored at 40° and 75% relative humidity. The formulation developed is simple, easy to prepare and economical with great applicability during the emergency cases such as allergic reactions, whenever immediate onset of action is desired.

**Key words:** Orally disintegrating, solvent-casting method, folding endurance, peel ability, Lycoat RS 720, pullulan, HPMC E5, kollicoat IR, monoammonium glycerrhizinate

For the past one decade, there has been an enhanced demand for more patient-friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increasing annually. Orally disintegrating films (ODF) have carved a niche amongst the oral drug delivery systems due to their high patient compliance<sup>[1-3]</sup>. United States Food and Drug Administration (USFDA) defined the fast dissolving oral thin films as “a thin, flexible, non-friable polymeric film strip containing one or more dispersed/dissolved active pharmaceutical ingredients, which is intended to be placed on the tongue for rapid *in vitro* disintegration or dissolution in the saliva prior to swallowing for delivery into the gastrointestinal tract”<sup>[4]</sup>.

Levocetirizine dihydrochloride, a third-generation non-sedative antihistamine developed as the active enantiomer of the second-generation antihistamine cetirizine. Levocetirizine is rapidly and extensively absorbed following oral administration with a plasma

elimination half-life ranging from 6-10 h<sup>[5]</sup>. In allergic cold and cough due to sore throat conditions, especially the elderly and paediatric, bedridden and non-cooperative patients experience difficulty in swallowing a tablet type of dosage form<sup>[6]</sup>.

The objective of the present research work was to develop taste masked ODF of levocetirizine dihydrochloride disintegrating within 30 s to enhance the convenience of administration to the patients to improve compliance. Various polymers like modified starch (Lycoat RS 720)<sup>[7,8]</sup>, pullulan<sup>[9,10]</sup>, hydroxypropyl methylcellulose (HPMC E-5)<sup>[11]</sup> and polyvinyl alcohol-polyethylene glycol (PEG) based polymer (Kollicoat

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IR)<sup>[12]</sup> were evaluated for film forming capacity. Plasticizers like glycerin, propylene glycol (PG), sorbitol and PEG 400<sup>[13]</sup> were evaluated by studying their effect on folding endurance, peelability and *in vitro* disintegration time of the polymer films. Pleasant tasting ODF of levocetirizine dihydrochloride were prepared in which bitter active was successfully taste masked by a mixture of sucralose and monoammonium glycerrhizinate producing an extended sweetness profile<sup>[7,14]</sup>. The formulation developed was simple, easy to prepare and economical with great applicability and also giving faster *in vitro* drug dissolution rate as compared to the commercially available immediate release tablets.

## MATERIALS AND METHODS

Levocetirizine dihydrochloride was gifted by Cipla Ltd. and sucralose was obtained from Ipca Labs. Polymers like pullulan were obtained from Gangwal Chemicals, Lycoat RS 720 from Roquette Pharma, HPMC E-5 from Colorcon Ltd., Kollicoat IR from BASF. monoammonium glycerrhizinate (Magnasweet) was obtained from Unicorn Natural Products Pvt. Ltd. All other chemicals and reagents were of analytical grade and were purchased from Loba Chemie, Mumbai.

### Screening of polymers for ODF:

Lycoat RS 720 (25%), pullulan (2-5%), HPMC E-5 (5-15%) and Kollicoat IR (2-15%) were evaluated as film forming agents and glycerin, PG, sorbitol and PEG 400 as plasticizers for their suitability in ODFs. Plasticizer was dissolved in small quantity of purified water and then the polymer was dissolved in it followed by deaeration by sonication. Films were cast on plastic petri plate and completely dried in oven at 60°.

The films were evaluated for film forming ability, folding endurance<sup>[15]</sup>, ease of peel ability, tackiness, uniformity and *in vitro* disintegration. The concentration of polymer, which formed smooth, homogeneous, non-tacky, flexible, fast disintegrating and easily peelable film was selected for formulation of drug-loaded film.

### Determination of threshold value of bitterness of levocetirizine dihydrochloride:

A panel comprising of six healthy volunteers (age 22-

25 y) were selected for this study. Prior consent has been taken from the participants as the study involved only holding the drug solution in the mouth for 30 s but not to swallow it. Then the solution was spitted out followed by rinsing the mouth with water. A series of solutions of levocetirizine dihydrochloride of concentrations 10, 20, 30, 40 and 50 µg/ml was prepared in phosphate buffer of pH 6.8. The volunteers were asked to hold 10 ml of each solution in oral cavity for 30 s and rate the taste on a scale from 0 to 4 (0: no bitterness, 1: threshold bitterness, 2: bitter, 3: moderate bitterness and 4: strongly bitter). The mouth was rinsed with distilled water and a gap of 30 min was allowed between successive tests. Based on opinion of volunteers, threshold bitterness concentration of levocetirizine dihydrochloride was determined. Various trials were taken by physical mixture of the drug with sucralose, with and without peppermint powder, with and without Magnasweet to mask the bitter taste of the drug and the ratings obtained have been shown in Table 1.

### Preparation of drug-loaded films:

Drug-loaded films were prepared by solvent casting method<sup>[16]</sup> for the optimized film compositions of each polymer. Levocetirizine dihydrochloride was incorporated at a concentration of 5 mg per 4 cm<sup>2</sup> film area. Amount of drug added into the film forming solution was calculated by considering total amount of solution to be poured in order to obtain films with desired thickness when casted on the calculated total surface area of the petri plate. Weighed quantities of the polymer and plasticizer were added to 3/4<sup>th</sup> the quantity of water, stirred until the polymer was dissolved and kept aside to remove the entrapped air. Levocetirizine dihydrochloride along with water soluble sweetener sucralose and monoammonium glycerrhizinate was dissolved in the remaining quantity of water and peppermint powder was then added to it under stirring. Both solutions were then mixed till a homogenous solution was obtained and then deaerated by sonication. Film was casted on plastic petri plate and completely dried at 60°. Dried films were peeled off and then stored in airtight container under dehumidified conditions until taken up for further evaluation.

**TABLE 1: TASTE ATTRIBUTES RATING SCALE**

Attributes	Rating scale			
	1- no	2- slight	3- extreme	-
After taste	1- not strong	2- moderate	3- strong	4- very strong
Flavour intensity	1- no bitterness	2- bitterness at the end	3- bitter	4- extremely bitter

### Evaluation of drug-loaded ODF:

The drug-loaded films obtained were evaluated for organoleptic and palatability characteristics. The thickness of each film was measured at five different locations (centre and four corners) using a vernier calliper. Data were represented as a mean $\pm$ SD of triplicate films. Films were cut into 2 $\times$ 2 cm square strips. The moisture uptake by the films was determined by exposing them to 75% relative humidity (RH) at room temperature (25 $\pm$ 2 $^{\circ}$ ) for one week<sup>[17]</sup>. The uptake of moisture by the films was measured and calculated as percent increase in weight. Tack is the tenacity with which the film adheres to an accessory that has been pressed into contact with the film. Tackiness evaluation<sup>[18]</sup> was carried out by gently pressing the film between fingertips and results were noted in qualitative terms as tacky or non-tacky. Film softening upon storage was checked by storing the films in desiccators at room temperature for 48 h. Films were then evaluated for softening and integrity.

The folding endurance of the film was determined by repeatedly folding one film at the same place till it broke. The number of times that film could be folded at the same place without breaking was noted; which gave the value of the folding endurance. *In vitro* disintegration time was determined by placing (2 $\times$ 2 cm<sup>2</sup>) film in a glass Petri dish containing 6 ml of distilled water. The time required for the film to break was noted as *in vitro* disintegration time. Typical disintegration time for ODFs is 5-30 s<sup>[19]</sup>. Test was conducted in triplicates. Drug content determination was done by dissolving three samples of 1 cm<sup>2</sup> surface area of film in 0.1 N hydrochloric and then analysing the amount of drug by UV spectrophotometer at 231 nm. The *in vitro* dissolution test was performed for each type of film using the USP dissolution apparatus II at 37 $\pm$ 0.5 $^{\circ}$  with stirring speed of 50 rpm in 900 ml 0.1 N hydrochloric acid and this was compared to the dissolution profile obtained with marketed immediate release tablets, Xyzal 5 mg under similar dissolution conditions. Film size required for dose delivery (2 $\times$ 2 cm<sup>2</sup>) was used. Five ml aliquot of dissolution medium was collected at time intervals of 1, 2, 5, 10, 15 and 30 min and replaced with equal volumes of 0.1 N hydrochloric acid. The collected samples were filtered and the concentration of the dissolved levocetirizine dihydrochloride was determined using UV spectrophotometer at 231 nm. The results were presented as an average of three such concentrations.

### Stability studies:

Stability studies of optimized batch of ODFs were performed under accelerated stability conditions (40 $\pm$ 2 $^{\circ}$ /75 $\pm$ 5% RH) kept in stability testing chamber for three months according to International Conference on Harmonisation (ICH) guidelines. The samples were evaluated for their physical characteristics, *in vitro* drug dissolution and assay initially and at the end of 1 and 3 mon of storage period.

## RESULTS AND DISCUSSION

The present study was undertaken to investigate polymers like Lycoat RS 720, pullulan, HPMC E-5 and Kollicoat IR for their film forming capacity. Preliminary trials (plain films) were undertaken for designing the orodispersible films where the effect of various concentrations of the different film-forming agents and plasticizers on the characteristics of the films was assessed. Initially investigation was focused on development of polymer films with uniform appearance, good peelability from substrate, non-tackiness, optimum flexibility, *in vitro* disintegration time of less than 30 s. Although no requirements for *in vitro* disintegration time have been specified for ODFs, a limit of 30 s was decided as a selection criterion for screening studies.

As per results of evaluation tests given in Table 2 and 3, Lycoat RS 720 at concentration of 25% w/w formed films with good peelability, while at lower concentration of 10% w/w, no film formation was observed. To impart flexibility and improve wetting property of Lycoat films, PG and polysorbate 80 were added. At 2% w/w concentration of PG, film was found to be brittle with low folding endurance. Hence PG concentration was increased to 4% w/w, which resulted in flexible film formation with good folding endurance. For both the trials, polysorbate 80 concentration was fixed i.e. 2% w/w. But Lycoat films were non-disintegrating at both the concentrations of PG; hence PG was replaced with sorbitol. Sorbitol was tried at 2% and 4% w/w concentration. It was observed that at 4% w/w concentration of sorbitol, film flexibility was maintained without affecting the stability. It was later found that in combination with soya lecithin, polysorbate was required in smaller concentration. 0.1% w/w polysorbate 80 and 0.8% w/w soya lecithin was incorporated in the films to aid in wetting and dissolution of film. No film softening upon storage was observed. Thus the polymer film of batch number

**TABLE 2: PHYSICO-MECHANICAL PROPERTIES OF LYCOAT RS 720 POLYMER FILMS**

Formulation	LF01	LF02	LF03	LF04	LF05
Film forming capacity	Poor	Poor	Very good	Good	Good
Peelability	Non-peelable	Non-peelable	Peelable	Brittle during peeling	Non-peelable
Appearance	Transparent	Transparent	Transparent	Transparent	Transparent
Tackiness	Non-tacky	Non-tacky	Non-tacky	Tacky	Non-tacky
Folding endurance	-	4	29	9	11
<i>In vitro</i> disintegration time (s)	Non-disintegrating	Non-disintegrating	Non-disintegrating	38	31
Film softening at 25°, 60% RH	Softening	Softening	Softening	No film softening	No film softening
Inference	No film formation	Brittle films Low folding endurance	Non disintegrating film	Brittle films	Non-peelable
Acceptability	No	No	No	No	No

**TABLE 3: PHYSICO-MECHANICAL PROPERTIES OF LYCOAT RS 720 POLYMER FILMS (CONTINUED)**

Formulation	LF06	LF07	LF08	LF09
Film forming capacity	Good	Good	Good	Very good
Peelability	Peelable	Peelable	Peelable	Peelable
Appearance	Transparent	Transparent	Transparent	Transparent
Tackiness	Tacky	Non-tacky	Slight tacky	Non-tacky
Folding endurance	28	20	33	31
<i>In vitro</i> disintegration time (s)	36	29	21	18
Film softening at 25°, 60% RH	No film softening	No film softening	No film softening	No film softening
Inference	Tacky	Folding endurance need to be improved	Slight tacky	Optimum
Acceptability	No	No	No	Yes

LF09 had acceptable film properties and hence it was selected for drug loading.

As per the results of evaluation tests given in Table 4; pullulan formed good peelable film at 2% w/w and 5% w/w concentration with *in vitro* disintegration time of less than 30 s. Hence lower concentration of pullulan was selected for further trials. Effect of different plasticizers was studied. Sorbitol was selected, which showed good folding endurance and no film softening. Thus 5% w/w pullulan film of batch number PF05 containing 0.5% sorbitol had acceptable film properties hence was selected for drug loading.

As per results of evaluation tests given in Table 5, HPMC E-5 formed good peelable film at 5% w/w. Effect of different plasticizers was studied at 0.7% concentration with 0.1% polysorbate. PG was selected as it gave the least D.T. Further trial was carried out with increasing concentration of HPMC from 5 to 7% to increase the thickness of the film along with 1% PG. *In vitro* disintegration time in 6 ml water was 10 s; hence HF05 was the optimized batch, which was selected for drug loading.

The present study revealed that Kollicoat IR did not form a film at 2% concentration but formed good peelable film at 5 and 10% w/w concentrations. Film softening was seen with 5% concentration of Kollicoat IR; hence 10% concentration was finalized. Polysorbate 80 (0.1%) was added as wetting agent. From the results as shown in Table 6, batch KF03 had acceptable film properties; hence it was selected for drug loading. Solvent casting being most preferred offered great uniformity and films had fine gloss and better physical properties. The films were easy to prepare without the use of organic solvents.

Most volunteers reported that 20 µg/ml as the threshold value of bitterness of levocetirizine dihydrochloride. This shows that the drug is extremely bitter and requires efficient taste masking method before formulating as orally disintegrating dosage forms. In order to ensure patient compliance and to allow the mouth disintegrating films to become a viable delivery system, bitterness masking becomes essential. Taste masking of levocetirizine dihydrochloride, which is extremely bitter was successfully achieved using a

**TABLE 4: PHYSICO-MECHANICAL PROPERTIES OF PULLULAN POLYMER FILMS**

Formulation	PF01	PF02	PF03	PF04	PF05
Film forming capacity	Good	Good	Good	Good	Very good
Peelability	Non-peelable	Peelable	Peelable	Brittle during peeling	Easily peelable
Appearance	Transparent	Transparent	Transparent	Opaque	Transparent
Tackiness	Non-tacky	Non-tacky	Tacky	Non-tacky	Non-tacky
Folding endurance	20	35	29	30	40
<i>In vitro</i> disintegration time (s)	28	16	20	18	15
Film softening at 25°, 60% RH	Softening	No film softening	Softening	Softening	No film softening
Inference	Low folding endurance	Good folding endurance	Brittle and tacky	Brittle films	Optimum
Acceptability	No	No	No	No	Yes

**TABLE 5: PHYSICO-MECHANICAL PROPERTIES OF HPMC E-5 POLYMER FILMS**

Formulation	HF01	HF02	HF03	HF04	HF05	HF06
Film forming capacity	Good	Good	Very good	Good	Very good	Poor
Peelability	Peelable	Peelable	Easily peelable	Peelable	Easily peelable	Non-peelable
Appearance	Transparent	Opaque	Transparent	Transparent	Transparent	Transparent
Tackiness	Non-tacky	Non-tacky	Non-tacky	Non-tacky	Non-tacky	Tacky
Folding endurance	20	22	35	25	40	-
<i>In vitro</i> disintegration time (s)	20	16	10	15	10	-
Film Softening at 25°, 60% RH	Softening	Softening	No film softening	Softening	No film softening	Softening
Inference	Low folding endurance	Film formed was not uniform	Less D.T compare to others	Brittle films	Optimum	Film was not formed
Acceptability	No	No	Yes	No	Yes	No

**TABLE 6: PHYSICO-MECHANICAL PROPERTIES OF KOLLICOAT IR POLYMER FILMS**

Formulation	KF01	KF02	KF03	KF04
Film forming capacity	Poor	Good	Very good	Poor
Peelability	Non-peelable	Peelable	Easily peelable	Non-peelable
Appearance	-	Transparent	Transparent	-
Tackiness	-	Non-tacky	Slight tacky	-
Folding endurance	-	30	37	-
<i>In vitro</i> disintegration time (s)	-	29	21	-
Film Softening at 25°, 60% RH	softening	softening	No film softening	softening
Inference	Film was not formed	Non-uniform film	Optimum	Film was not formed
Acceptability	No	No	Yes	No

combination of sucralose as the sweetener, peppermint as flavour and monoammonium glycerhizinate as the flavour enhancer and bitter taste masking agent. Sucralose as a sweetener has an initial burst of sweetness, which dissipates rapidly but in combination with monoammonium glycerhizinate, which is a flavour enhancer produced a sweetness profile that extended itself over the time of the product being

experienced in the mouth. From the scores given by volunteers for the taste masking trials (Table 7); the batch F03 with sucralose 2 mg, peppermint powder 2 mg and monoammonium glycerhizinate 0.2 mg was selected as effectively taste masked batch.

Drug loading in the optimized formula for each polymer (Table 8) was successful without any change in film characteristics. Results of evaluation tests performed for

the characterization of levocetirizine dihydrochloride ODFs are given in Table 9. Films of formula LODF01 were non-tacky, smooth and transparent with thickness of 0.2 mm. Also *in vitro* dissolution time of this film was within 30 s; hence it was observed that drug loading did not affect the properties of Lycoat polymer films. Drug-loaded pullulan film was non-tacky, transparent and disintegrated in 15 s. HPMC E-5 film containing levocetirizine dihydrochloride disintegrated within 10 s. Film obtained was non-tacky, transparent and folding endurance was 40. Drug-loaded Kollicoat IR film was non-tacky, flexible, and transparent and disintegrated within 21 s. Kollicoat IR consists of 75% polyvinyl alcohol and 25% of PG hence there was no need for additional plasticizer.

*In vitro* dissolution study of all the batches showed >95 % drug dissolution in 10 min, whereas the marketed immediate release tablets of levocetirizine dihydrochloride, Xyzal 5 mg tablets shows only 30.4% dissolution in 10 min and 101.9% dissolution in 30 min (fig. 1). It was found that the optimized formulations were stable for at least three months at accelerated condition ( $40\pm 2^\circ/75\pm 5\%$  RH) as no significant change in appearance, thickness, folding endurance, *in vitro* disintegration time, drug content and *in vitro* dissolution time and extent was observed (Table 10 and 11).

Lycoat RS 720 (25%), pullulan (5%), HPMC E-5 (7%) and Kollicoat IR (5%) of levocetirizine formed flexible, peelable, transparent fast dissolving films weighing

around 50 mg and showing disintegration time within 30 s. The films showed faster drug release and dissolution as compared to commercial immediate release tablets and were attractive in appearance and produced sweet after taste, thus fulfilling the objectives of the present research work. These ODF can yield significantly better or at least comparable pharmacokinetic profile ( $AUC$ ,  $T_{max}$ ,  $C_{max}$ ) as the conventional immediate release solid dosage forms<sup>[20]</sup> and hence may prove to be more efficacious. The present research work demonstrated that the bitter taste of water soluble drug levocetirizine dihydrochloride can be completely eliminated by a combination of sucralose, peppermint powder and monoammonium glycerhizinate, which

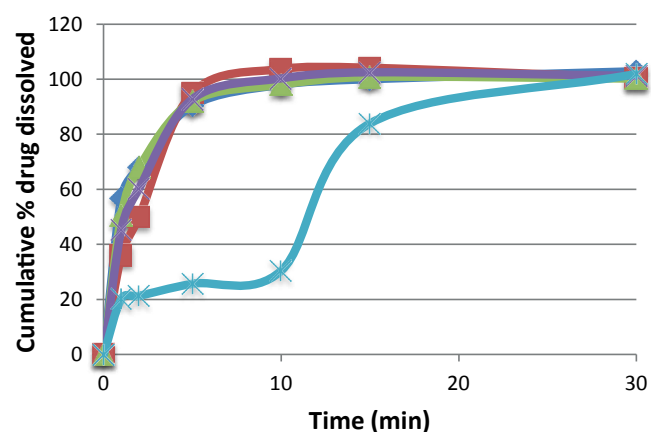


Fig. 1: *In vitro* drug dissolution profile of ODF vs. immediate release marketed tablet  
 —◆— LODF01; —■— LODF02; —▲— LODF03; —×— LODF04; —\*— IR marketed tablets

TABLE 7: TASTE SCORING GIVEN BY VOLUNTEERS

Batch No	After taste	Flavour intensity	Bitterness
F01	3	1	3
F02	2	1	3
F03	1	2	1

TABLE 8: OPTIMIZED COMPOSITION OF LEVOCETIRIZINE DIHYDROCHLORIDE ODF

Ingredients	Concentration (%w/w)			
	LODF01 (Lycoat RS 720)	LODF02 (Pullulan)	LODF03 (HPMC E-5)	LODF04 (Kollicoat IR)
Lycoat RS 720	25	-	-	-
Pullulan	-	5	-	-
HPMC E-5	-	-	7	-
Kollicoat IR	-	-	-	10
Polysorbate 80	0.1	0.1	0.1	0.1
Soy lecithin	0.8	-	-	-
Sorbitol	4	0.5	-	-
Propylene glycol	-	-	1	-
Sucralose	1	1	1	1
Monoammonium glycerhizinate	0.1	0.1	0.1	0.1
Peppermint powder	0.8	0.8	0.8	0.8
Purified water	q.s.	q.s.	q.s.	q.s.

**TABLE 9: PHYSICO-CHEMICAL PROPERTIES OF LEVOCETIRIZINE DIHYDROCHLORIDE ODF**

PARAMETERS	LODF01 LYCOAT	LODF02 PULLULAN	LODF03 HPMC E-5	LODF04 KOLLICOAT IR
Appearance	Smooth surface and transparent	Smooth surface and transparent	Smooth surface and transparent	Smooth surface and transparent
Taste	Sweet and minty smooth taste	Sweet and minty smooth taste	Sweet and minty smooth taste	Sweet and minty smooth taste
Tack test	Non-tacky	Non-tacky	Non-tacky	Non-tacky
%Moisture uptake	0.46	0.6	0.82	0.62
Thickness (mm)	0.2	0.2	0.2	0.2
<i>In vitro</i> disintegration time (s)	18	15	10	21
Folding endurance	31	40	40	37
Film softening upon storage	No film softening	No film softening	No film softening	No film softening
%Drug content	98.29	101.36	99.2	102
Inference	Acceptable	Acceptable	Acceptable	Acceptable

**TABLE 10: STABILITY DATA OF LYCOAT AND PULLULAN ODF**

Physical parameters	Conditions (°/%RH)	LODF01 (Lycoat RS 720)			LODF02 (Pullulan)		
		Initial	30 <sup>th</sup> day	90 <sup>th</sup> day	Initial	30 <sup>th</sup> day	90 <sup>th</sup> day
Appearance	40/75	Transparent	Transparent	Transparent	Transparent	Transparent	Transparent
	25/60	Transparent	Transparent	Transparent	Transparent	Transparent	Transparent
Thickness (mm)	40/75	0.2 mm	0.2 mm	0.2 mm	0.2 mm	0.2 mm	0.2 mm
	25/60	0.2 mm	0.2 mm	0.2 mm	0.2 mm	0.2 mm	0.2 mm
Folding endurance	40/75	31	30	32	40	38	36
	25/60	32	29	30	35	33	30
% Moisture uptake	40/75	0.45	0.4	0.42	0.6	0.55	0.58
	25/60	0.52	0.42	0.48	0.55	0.5	0.48
<i>In vitro</i> disintegration time (s)	40/75	18	20	18	20	18	20
	25/60	20	22	20	20	22	20
Assay %	40/75	98	98.5	101.5	101	102.2	102
	25/60	99	101	100.2	102	101.5	100.5

**TABLE 11: STABILITY DATA OF HPMC AND KOLLICOAT ODF**

Physical parameters	Conditions (°/%RH)	LODF03 (HPMC)			LODF04 (Kollicoat)		
		Initial	30 <sup>th</sup> day	90 <sup>th</sup> day	Initial	30 <sup>th</sup> day	90 <sup>th</sup> day
Appearance	40/75	Transparent	Transparent	Transparent	Transparent	Transparent	Transparent
	25/60	Transparent	Transparent	Transparent	Transparent	Transparent	Transparent
Thickness (mm)	40/75	0.2 mm	0.2 mm	0.2 mm	0.2 mm	0.2 mm	0.2 mm
	25/60	0.2 mm	0.2 mm	0.2 mm	0.2 mm	0.2 mm	0.2 mm
Folding endurance	40/75	40	38	36	37	38	36
	25/60	35	36	30	32	30	35
%Moisture uptake	40/75	0.8	0.78	0.8	0.6	0.62	0.6
	25/60	0.58	0.6	0.65	0.58	0.58	0.65
<i>In vitro</i> disintegration time (s)	40/75	20	22	20	20	25	22
	25/60	25	22	24	22	23	21
Assay %	40/75	99	100	101.5	101	102.2	102
	25/60	98	101.5	100.2	99.5	101.2	100.8

can also give extended sweetness profile. Thus the development of paper thin ODF providing all the homogeneity advantages of a liquid formulation with convenience and stability of a solid dosage form can be

a viable option when rapid action is required especially in case of non-cooperative patients.

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### Conflict of interest:

There are no conflicts of interest.

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### REFERENCES

1. Aurora J, Pathak V. Oral disintegrating dosage forms, an overview. *Drug Del Tech* 2005;5:50-54.
2. Bala R, Pawar P, Khanna S, Arora S. Orally dissolving strips: a new approach to oral drug delivery system. *Int J Pharm Investig* 2013;3:67-76.
3. Kathpalia H, Gupte A. An introduction to fast dissolving oral thin film drug delivery system: a review. *Curr Drug Deliv* 2013;10:667-84.
4. [http://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2015/022524orig1s000chemr.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/022524orig1s000chemr.pdf).
5. <https://www.drugbank.ca/drugs/DB06282>.
6. Hirani J, Rathod D, Vadalía K. Orally Disintegrating Tablets: A Review. *Trop J of Pharm Res* 2009;8:161-72.
7. Kathpalia H, Sule B, Gupte A. Development and evaluation of orally disintegrating film of tramadol hydrochloride. *Asian J Biomed Pharm Sci* 2013;3:27-32.
8. Preis M, Pein M, Breitreutz J. Development of a taste-masked orodispersible film containing dimenhydrinate. *Pharmaceutics* 2012;4:551-62.
9. Foss D, Hoffman A, Shen S, Stucky AM, Turner JL. Edible pullulan films containing flavouring. US Patent Number-US20090011115A1;2009.
10. Renuka M, Avani A. Formulation and characterization of rapidly dissolving films of cetirizine hydrochloride using pullulan as a film forming agent. *Indian J Pharm Educ Res* 2011;45:72-7.
11. Daud A, Bonde M, Sapkal N, Gaikwad N. To study the effect of solvent, viscosity and temperature on mouth dissolving film of *Withania somnifera* linn. *Asian J Pharm* 2012;6:212-7.
12. 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.
13. Mishra R, Amin A. Formulation development of taste masked rapidly dissolving films of cetirizine hydrochloride. *Pharm Tech* 2009;33:48-56.
14. Myers GL, Hariharan MS, Davidson K, Sanghvi P. Stabilized amine-containing actives in oral film composition. US Patent Number-US9095577 2015;2015.
15. Panda BP, Dev NS, Rao MEB. Development of innovative orally fast disintegrating dosage forms: a review. *Int J Pharm Sci Nanotech* 2012;5:1666-74.
16. Hoffmann EM, Breitenbach A, Breitreutz J. Advances in orodispersible films for drug delivery. *Expert Opin Drug Deliv* 2011;8:299-316.
17. Radhakishan UR, Chavan V, Tribhuvan N. Mouth dissolving films and their patents: An overview. *Int Res J Pharm* 2012;3:39-42.
18. Bhupinder B, Sarita J, Mandeep K, Harmanpreet S. Orally fast dissolving films: innovations in formulation and technology. *Int J Pharm Sci Rev Res* 2011;9:50-4.
19. Barnhart S. Thin film oral dosage forms. In: Rathborne MJ, Hadgraft J, Roberts MS, Lane ME, editors. *Modified release drug delivery technology: Drugs and the pharmaceutical sciences*. 2nd ed. New York: Marcel Dekker; 2008. p. 209-16.
20. Zhang H, Chen H, Li XJ, Zhang Q, Sun YF, Liu CJ, *et al.* Pharmacokinetics and safety profiles of novel diethylstilbestrol orally dissolving film in comparison with diethylstilbestrol capsules in healthy Chinese male subjects. *Int J Clin Pharmacol Ther* 2014;52:407-15.