FORMULATION AND EVALUATION OF FAST DISSOLVING FILMS OF OLOPTADINE HCL

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ABSTRACT

Our studies on the performance of formulation and evaluation of fast dissolving films of Olopatadine HCL its anti-allergic drug. Prepare mouth dissolving film of Olopatadine HCl by solvent casting method. To characterize the prepared mouth dissolving film of Olopatadine HCL in terms of— Thickness, percent elongation, tack test, swelling index, in-vitro disintegration time and dissolution test. Olopatadine OLO), 11-[{z}-3-(Dimethlamino) propylidene]-6-11-dihydrobenz [b, e] oxepin-2-acetic acid hydrochloride, is widely used as an antihistaminic. Olopatadine HCL is a relatively selective histamine H1-receptor antagonist that inhibits the release of histamine from mast cells. Olopatadine does not affect alpha-adrenergic dopamine, muscarinic type 1 and 2 or serotonin receptor. They are hydrophobic in nature and non-polar, sparingly soluble in water and freely soluble methanol, ethanol. Olopatadine HCl is a mouth dissolving film. We is trying to sort out the problem of allergic. They are rapidly onset of action, when placed upon the tongue that it is disperse rapidly swallowing within 3-5 seconds without need of water or chewing.

KEYWORDS: Fast dissolving film, solvent casting method, freely soluble, onset of action.

1. INTRODUCTION:

Fast dissolving oral films are the most advanced form of oral solid dosage form due to more flexibility and comfort. It improve the efficacy of active pharmaceutical ingredients' (Al'ls) by dissolving within minute in oral cavity after the contact with saliva without chewing or no need of water for administration. It gives quick absorption and instant bioavailability of drugs due to high blood flow and permeability of oral mucosa is 4-l000 time greater than that of skin.

Recent development in the technology has presented viable dosages alternatives from oral routes for pediatrics. Geriatric, bedridden, nauseous or non, compliant patient. Fast dissolving drug delivery systems were first developed in the late 1970s as an alternative to tablet, capsule and syrup for pediatric and geriatric patient 'who experience difficulties swallowing traditional oral solid dosage forms.

In US market OTC films of pain management and motion sickness are commercialized. More importantly, prescription OTFs have nowbeen approved in US, EU and Japan which are the three major regions. These approved Rx films, have potential dominate over dosage forms of the same drugs, it seems that the value of the oral thin films market will grow significantly.

2. RELATED WORK:

In this work authored described about, give an idea on to prepare films. Salicylic acid and theophylline were incorporated into cast chitosan Films as model acidic and basic drugs.[1] the penetration rate of Lidocaine (LC) through excised oral mucosa from hamster cheekpouch and the in vitro release rate of LC from film dosage forms with hydroxypropylcellulose (HPC) as a film base[2] developed a

fast-dissolving film made of low dextrose Equivalent maltodextrins (MDX) containing nicotine hydrogen tartrate salt[3] prepared fast dissolving film of piroxicam using maltodextrin with low dextrose equivalent as film forming using casting and solvent evaporation method. Fast dissolving films of piroxicam showed high loading capacity of dose with dissolution rate.[4] The fast dissolving films of rofecoxib by solvent casting method by use of HPMC as polymer. They concluded that mouth dissolving films containg rofecoxib 4%w/v of PVA film exhibited revive tensile strength, folding endurance and percentage elongation.[5]

3. METHOD AND MATERIALS:

Materials-

1. Olopatadine HCL
2. Hydroxy propyl methyl cellulose (HPMC-15)
3. Maltodextrin (DE-20)
4. Propylene glycol
5. Glycerin
6. Menthol
7. Di sodium hydrogen phosphate
8. Potassium dihydrogen phosphate
9. Sodium
10. Ethanol
11. Methanol

METHOD-

One of the following processes may be used to manufacture the oral films-

1- SOLVENT CASTING METHOD:

Fast dissolving buccal films are preferably formulated using the solvent casting method, where by the water soluble ingredient are dissolved to form a clear viscous solution and the drug along with other excipients is dissolved in suitable solvent then both the solutionsare mixed and stirred and finally casted into the Petri plate and dried.

2- HOTMELT EXTRUSION:

Usually, when designing RDFs, polymers with low molecular weight or viscosity, such as HPMC E5, HPMC E15 and Malt dextrin arepreferred. A combination of various grades of polymer may also be used to achieve desired physical properties.

3- SEMISOLID CASTING METHOD:

Solution of water soluble film forming polymer is prepared resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate, cellulose acetate butyrate) appropriate amount of plasticizers is added so that gels mass obtained finally the gel mass is casted into the films or ribbons using heat controlled drums. The thickness of the films should be about 0.015-0.05inches.

4- ROLLING METHOD:

In this method the films is prepared by preparation of a pre-mix, addition of an active and subsequent formation of a film

EVALUATION:

The fast dissolving films of Olopatadine HCL were evaluated for the following properties-

1. Morphology of film
2. Foulding endurance of film
3. Surface of pH of film
4. Petridis method
5. Percent elongation
6. Tensile strength
7. Weight uniformity of film
8. Thickness of film
9. Drug content uniformity

4. EXPERIMENTS AND RESULTS:

METHOD DEVELOPMENT:

1. Determination of solubility.
2. Selection of solvent system.
3. Study of spectra of drug and selection of suitable method.
4. Wavelength selection for linearity study.
5. Linearity range and calibration graph.

1.SOLUBILITY:
Solubility of drug was observed by dissolving in different solvents.

TABLE 1- SOLUBILITY OF OLOPTADINE HCL

S. No	Solvent	Solubility of Drug Oloptadine HCl
1	Water	Sparingly Soluble
2	Methanol	Soluble
3	Ethanol	Soluble
4	Acetone	Soluble
5	Acetonitrile	Soluble

2.SELECTION OF SOLVENT SYSTEM:
The solution of Oloptadine HCl were prepared in various solvent systems and scanned over the UV range (200-400) in spectrum modeat slow scan speed, distilled water and Methanol was selected as the best solvent system. The Methanol is selected because-

1. Drug is soluble in it.
   Drug is stable in it

3.STUDY OF SPECTRA AND SELECTION OF SUITABLE METHOD:
From stock solution concentration of 10µg/ml for Oloptadine HCL was prepared. Drug was scanned over the range of 200-400nm,while studying the spectra it was observed that Oloptadine HCL shows maximum absorbance at 290.5nm, drug can be estimated by simple direct measurement of absorbance at its $\lambda_{max.}$

4.SELECTION OF WAVELENGTH FOR LINEARITY:
The wavelength was selected, to study the linearity of Olopatadine HCL in the maximum absorbance maxima (λ_{max}). i.e. λ maxof Olopatadine HCl: 290.5nm

5.LINEARITY AND CALIBRATION GRAPH:
[A] LINEARITY RANGE:
Different dilutions of Olopatadine HCl between 0-100 µg/ml were scanned at their λmax in UV range and found that OlopatadineHCl follow linearity between **2-**10µg/ml.

[B] CALIBRATION GRAPH:
Accurately weighed 50mg Olopatadine HCl was transferred into 50ml volumetric flask and dissolved in Methanol, then volume was made up to 50ml with Distilled Water to get a concentration of 1000µg/ml (Stock-A). 2.5ml of stock-A of Olopatadine HCl was taken in25ml volumetric and diluted up to 25ml to get concentration of 100µg/ml (Stock-B). Finally from stock solution-B different of 2, 4, 6,8 and 10µg/ml were prepared for analysis. Absorbance's were observed at 290.5nm. Linearity was observed by the linear regression equation and correlation coefficient was found to be 0.999.

PREPARATION OF STANDARD SOLUTION FOR CALIBRATION GRAPH:
From the stock solutions B aliquots diluted up to 25 ml with Distilled water to obtain the concentrations

TABLE 2-: PREPARATION OF STANDARD SOLUTION FOR CALIBRATION GRAPH

Volume taken in Ml from Stock B	Conc. (µg/ml)
0.5	2
1.0	4
1.5	6
2.0	8
2.5	10

TABLE 3-: LINEARITY FOR AT 290.5NM

Conc. (µg/ml)	Absorbance at 290.5nm						
	Rep 1	Rep 2	Rep 3	Rep 4	Rep 5	Mean	S. D
2	0.0732	0.0739	0.0722	0.0738	0.0742	0.0731	0.001647
4	0.1492	0.1482	0.1473	0.1460	0.1455	0.14724	0.001527
6	0.2212	0.2112	0.2310	0.2210	0.2312	0.22312	0.008331
8	0.3012	0.3011	0.3022	0.3018	0.3014	0.30154	0.000456
10	0.3655	0.3659	0.3650	0.3645	0.3657	0.36532	0.000567

R^2	0.9990	0.9997	0.9994	0.9998	0.9995
Slope	0.073	0.074	0.076	0.070	0.073
Intercept	0.001	0.001	0.001	0.001	0.001

STANDARDIZATION OF THE METHOD:

In order to confirm the validity of the method, laboratory samples containing Olopatadine HCl were prepared, in the range of 2µg – 10µg/ml. The amount of drug present in the standard solution was calculated by using the selected linearity equation and the results aretabulated.

TABLE 4: DATA FOR LABORATORY SAMPLES ANALYSIS

S.No	Conc. of drug(µg/ml)	Replicate	Abs at 290.5nm	Concentration Found	% Mean
1	2	i	0.0732	1.99	98.1
		ii	0.0739	1.98	
		iii	0.0722	1.92	
2	6	i	0.2212	5.97	99.72
		ii	0.2112	5.97	
		iii	0.2310	6.01	
3	10	i	0.3655	9.89	98.83
		ii	0.3659	9.97	
		iii	0.3650	9.79	
				Mean	98.88
				S.D.	0.8113

ANALYSIS OF FORMULATION:

Formulation that was used for analysis (OLPD film) contains 2mg Olopatadine HCL per film. For analysis, accurately weighed there average weight was determined and dissolved in methanol equivalent to 2mg of Olopatadine HCL film was accurately weighed and transferred to a volumetric flask and made up to the mark with the solvent. This solution was sonicated for 20 min and filtered through whatman filter paper (41 numbers) to get a solution of 1000µg/ml. Further diluted samples in the range of 2µg – 10µg/ml were prepared.

The amount of drug present in the sample solution was calculated by using the selected linearity equation and the results are in the Table

TABLE 5: DATA FOR FILM ANALYSIS

S. No	Conc. of drug (µg/ml)	Replicate	Abs at 290.5 nm	Concentration Found	% Mean
1	2	i	0.0738	1.96	98.61
		ii	0.0737	1.97	
		iii	0.0732	1.99	
2	6	i	0.2214	5.79	99.72
		ii	0.2120	5.88	
		iii	0.2332	6.1	
3	10	i	0.3660	9.94	98.33
		ii	0.3624	9.87	
		iii	0.3698	9.99	
				Mean	98.88
				S.D.	0.7689

METHOD VALIDATION:

LINEARITY:

The linearity of a method is a measure of how well a calibration plot of response versus concentration approximates a straight line. Linearity range for any drug refers to that concentration range in which it follow the Beer Lamberts law that states, "The absorbance of a solution is directly proportional to the concentration of the absorbing species when the length of the light path is fixed and directly proportional light path when the concentration is fixed". For establishing the linearity range samples of five concentration of Olopatadine HCL in the range of 2µg – 10µg/ml in three replicas was prepared as: From Stock-B further diluted samples (5 replicates) in the range of 2µg – 10µg/ml were prepared. The results obtained were interpreted for any variation and data was statistically validated.

TABLE 6: RESPONSE RATION DATA FOR LINEARITY

S. No.	Concentration (µg/ml)	Absorbance	Response Ratio
1	2	0.0732	0.0366
2	4	0.1492	0.0373
3	6	0.2212	0.0368
4	8	0.3012	0.0376
5	10	0.3655	0.0365
Mean			0.0369
S.D.			0.00047

ACCURACY (RECOVERY STUDIES):

To test accuracy, recovery studies were performed. To a preanalyzed sample solution, a definite concentration of standard drug was added and then its recovery was studied. Different concentration of pure drug was added to preanalysed tablet sample, and then the solution was analyzed in the same manner as the laboratory sample. It was repeated for three times to emphasize validation. Results of recovery study were reported.

TABLE 7: RECOVERY STUDY DATA FOR ACCURACY OF OLOPATADINE HCL

S. No.	Conc. of Drug in film(µg/ml)	Replicates	Conc. added to the film samples (µg/ml)	Amount Recovered	% Found
1	4	i	2	1.93	98.21
		ii	2	1.89	
		iii	2	1.98	
2	4	i	4	4.01	99.55
		ii	4	3.98	
		iii	4	3.88	
3	4	i	6	6.02	98.29
		ii	6	5.89	
		iii	6	5.76	
				Mean	98.68
				S.D.	0.6789
				%CV	

TABLE 8: INTERMEDIATE PRECISION: ANALYST TO ANALYST

S. No	Conc. of drug(µg/ml)	Replicate	Abs at 290.5nm	Concentration Found	% Mean
1	2	i	0.0722	1.44	80.33
		ii	0.0798	1.89	
		iii	0.0712	1.49	
s2	4	i	0.1482	3.55	98.36
		ii	0.1428	3.92	
		iii	0.1483	3.91	
3	6	i	0.2222	5.78	99.14
		ii	0.2132	5.56	
		iii	0.2320	5.89	
4	8	i	0.3027	7.69	98.96
		ii	0.3034	7.77	
		iii	0.3052	7.79	
5	10	i	0.3657	9.98	99.61
		ii	0.3642	9.87	
		iii	0.3648	9.97	
				Mean	
				S.D.	1.31

PRECISION:

REPEATABILITY:

As per section 5.1.3.5 standard dilutions were prepared and three replicates of each dilution were analyzed in same day for repeatabilityof precision. Statistical analysis was carried out.

INTERMEDIATE PRECISION:

Standard dilutions were prepared in three replicates and were analyzed in different days by different analysis. Statistical analysis wascarried out.

5. CONCLUSION:

In the present work, fast dissolving film of olopatadine HCl were prepared by solvent casting method using HPMC E-15, Maltodextrin 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 disintegration time of film was reduced by use of maltodextrin with HPMC E-15 as a combination from the finding obtained it can be concluded that-

The prepared film containing olopatadine HCl was clear and colorless.

1 Formulated film gives satisfactorily results for various physicochemical evaluation of film like physical appearance, surface texture, weight uniformity, thickness, folding endurance surface PH in-vitro disintegration time drug release, the value of standard deviation for average weight and drug content of the prepared films indicate weight and drug content uniformity within the batches prepared. Short term stability studies of promising formulation indicated that there is no significant change in drug content and in-vitrodisintegration time.

2 From the present study it may be concluded that fast dissolving films of olopatadine HCl can be prepared by solvent castingmethod using HPMC and Maltodextrin.

6. REFERENCES:

1. Puttipipatkhachorn S etal (2001) conducted studies on four different grades of chitosan to prepare films. Salicylic acid and theophylline were incorporated into castchitosan Films as model acidic and basic drugs.
2. Hirokazu O etal (2001) examined the penetration rate of Lidocaine (LC) through excised oral mucosa from hamster cheek pouch and the in vitro release rate of LC from film dosage forms with hydroxypropylcellulose (HPC) as a film base.
3. Francesco C etal (20l0), developed a fast-dissolving film made of low dextrose Equivalent maltodextrins (MDX) containing nicotine hydrogen tartrate salt.
4. Cillurzo F et al. (2008) prepared fast dissolving film of pioxicam using maltodextrin with low dextrose equivalent as film forming using casting and solvent evaporation method. Fast dissolving films of piroxicam showed high loading capacity of dose with dissolution rate.
5. Kulkarni et al (2009) take the fast dissolving films of rofecoxib by solvent casting method by use of HPMC as polymer. They concluded that mouth dissolving films containg rofecoxib 4%w/v of PVA film exhibited revive tensile strength, folding endurance and percentage elongation.