Formulation & Evaluation of Loratadine Hydrochloride Oral Disintegrating Tablets by Direct Compression Method by Using super Disintegrates

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ABSTRACT :-

The objective of the present study was to prepare oral disintegrating tablets of a loratadine hydrochloride using solid dispersion. Loratadine hydrochloride is a derivative of azatadine class of antihistamic drug which belongs to BCS-II having low solubility and high permeability. One of the major problems with this drug is its low solubility in biological fluids, which results in poor bioavailability after oral administration. The solubility of poorly soluble drug was enhanced by preparing solid dispersions of the drug by using hydrophilic polymers PEG 6000 and urea carriers in the ratios of 1:1, 1:2, 1:3, 1:4 and 1:5 respectively by fusion method. The optimized solid dispersions were further kneaded with suitable proportions of super disintegrates such as Cross-povidone, sodium starch glycolate and croscarmellose sodium and different diluents micro crystalline cellulose and lactose. Oral disintegrating tablets of loratadine hydrochloride were prepared by direct compression method. The results of FT-IR spectroscopy showed that there was no interaction between the drug and excipients. The prepared formulations were evaluated for weight variation, thickness, hardness, friability, wetting time, water absorption ratio, in-vitro disintegration time and in-vitro dissolution studies. The optimized formulation was found to be F15 (formulation with cross povidone and lactose as diluent). It was concluded that oral disintegrating tablets of loratadine hydrochloride prepared by solid dispersions of drug with urea and lactose as diluent and cross povidone as super disintegrate provide complete and better dissolution within in shorter period of time. Hence effective allergic treatment anywhere, and anytime particularly for geriatric, pediatric, mentally ill, bedridden and patients who do not have easy access to water.

Key Words *:- PEG 6000, Loratadine hydrochloride, oral disintegrating.*

INTRODUCTION

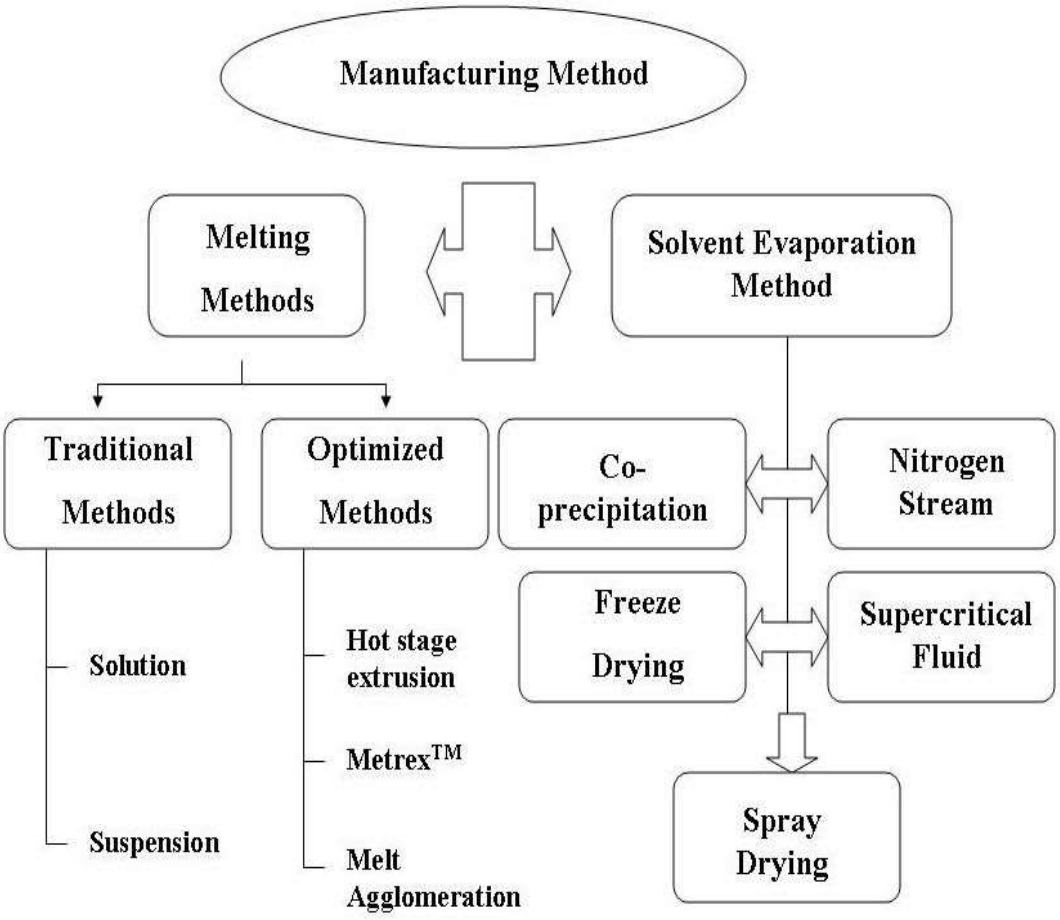
Drug delivery through oral route is the most common and preferred route of drug administration both for solid and liquid dosage forms. However, solid dosage forms are popular because of the ease of administration, accurate dosage, self-education, pain avoidance, and most importantly the patient compliance. Tablets and capsules are the most popular solid dosage forms[1.] However, many people face difficulty in swallowing tablets and hard gelatin capsules[6]. This difficulty swallowing is called dysphasia[2, 3]. It has been found that this problem has been encountered in all groups of patients, but especially with pediatric and geriatric populations. Thus, these conventional dosage forms result in high incidence of noncompliance and ineffective therapy with respect to swallowing specially in the case of pediatric geriatric or any mentally retarded persons. Oral dispersible tablets (ODTS) are also called as orally disintegrating tablets, mouth dissolving tablets, rapid-dissolving tablets, fast-disintegrating, fast dissolving tablets.[1, 2]

SOLUBILITY INTRODUCTION

Solubility is the property of a solid, liquid, or gaseous chemical substance called solute to dissolve in a solid, liquid, or gaseous solvent to form a homogeneous solution of the solute in the solvent. It is defined as the phenomenon of dissolution of solute in solvent to give a homogenous system. It is one of the important parameters to achieve desired concentration of drug in systemic circulation for desired pharmacological response. Low aqueous solubility is the major problem encountered with formulation development of new chemical entities as well as for the generic development.

Methods of Preparation of Solid Dispersions

- Fusion method
- solvent evaporation method
- Melting solvent method
- Melt extrusion method
- Lyophilization Technique
- Melt Agglomeration Process
- Use of surfactant
- Electrospinning
- Super Critical Fluid Technology



Methods of preparation of Solid Dispersion

ORAL DISINTEGRATING TABLETS (ODT)

Definition[1, 4]

The Centre for Drug Evaluation and Research (CDER), USFDA defines ODT as "a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds when placed upon the tongue". European Pharmacopoeia described orally disintegrating tablets as "uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed and as tablets which should disintegrate within 3 min". Oral disintegrating tablets were kept on tongue where they get dispersed in saliva, resulting in a solution or suspension without the need of water or chewing.

Ideal properties of ODTs[6, 7]

- Require no water for oral administration, yet dissolve/disperse/ disintegrate in mouth in a matter of seconds.
- Have a pleasing mouth feel, have an acceptable taste masking property, Be harder and less friable
- Leave minimal or no residue in mouth after administration. Exhibit low sensitivity to environmental conditions (temperature and humidity).
- Allow the manufacture of tablet using conventional processing and packaging equipment's.

TECHNIQUES IN PREPARATION OF ORALLY DISINTEGRATING DRUG DELIVERY SYSTEM[7, 11]

1. Freeze drying or Lyophilization
2. Spray drying
3. Molding
4. Phase transition process
5. Melt granulation
6. Sublimation
7. Mass extrusion
8. Cotton candy process
9. Direct compression
10. Nano ionization
11. Effervescent method

MATERIALS & METHODS :-

List of Raw Materials:-

S. No	Name of Ingredients	Name of supplier
1	Loratadine hydrochloride	Reddy's Laboratories
2	Cross povidone	Nihal Traders Pvt Ltd, Hyderabad
3	Sodium starch glycolate	Corel Pharma Chem, Hyderabad
4	Microcrystalline Cellulose pH102	Central Drug House (P) Ltd, New Delhi
5	Lactose monohydrate	Qualikems Fine Chemicals, Pvt, Ltd, Vadodara
6	Croscarmellose sodium	Central Drug House (P) Ltd, New Delhi
7	PVP-K30	Central Drug House (P) Ltd, New Delhi
8	PEG 6000	Qualikems Fine Chemicals, Pvt, Ltd, Vadodara
9	Urea	Dr. Reddy's Laboratories
10	Talc	Central Drug House (P) Ltd, New Delhi
11	Magnesium stearate	Central Drug House (P) Ltd, New Delhi

Preparation of Solid dispersions of Loratadine hydrochloride[12, 13]

Solid dispersions of the drug were prepared by fusion method using urea and PEG 6000 as carriers.

Fusion method: Solid dispersions were prepared by fusion method with different ratios of Loratadine hydrochloride and carriers (1:1, 1: 2, 1:3, 1:4 and 1:5). In fusion method carrier was melted and then to the melted carrier drug was added slowly by continues trituration for uniform mixing and then solidified rapidly in an ice-bath.

Preparation of solid dispersion

Carrier	Drug : Carrier ratio
Urea	1:1
	1:2
	1:3
	1:4
	1:5
PEG 6000	1:1
	1:2
	1:3
	1:4
	1:5

Preparation of oral disintegrating tablets of Loratadine hydrochloride[14, 15, 16]

Direct compression technique was used to prepare the tablets. It is the simplest and most economical method for the manufacturing of tablets because it requires less processing steps than other techniques such as wet granulation and roller compaction. The optimized solid dispersions (Drug: urea in 1:5 ratio by fusion method) equivalent to 10mg of Loratadine hydrochloride was mixed with aerosol which acts as an adsorbent. To this powder different concentrations of cross povidone, sodium starch glycolate and croscarmellose sodium super disintegrates were added along with the other excipients PVP k_{30} as binder and avicel and lactose as diluents respectively. They were sieved through 20# screen and mixed for 10min to obtain uniform mixing. Finally, 1% talc was mixed for lubrication which was then directly compressed into fast dissolving tablets by rotary compression machine using 6mm flat punch.

Composition of Loratadine hydrochloride oral disintegrating tablets :-

Formulations	SD Equivalent to Drug (mg)	SSG (mg)	CP (mg)	CCS (mg)	Lactose	MCC	PVP K_{30}	Total weight
F1	60	2	-	-	27	-	5	100
F2	60	4	-	-	25	-	5	100
F3	60	6	-	-	23	-	5	100
F4	60	-	2	-	27	-	5	100
F5	60	-	4	-	25	-	5	100
F6	60	-	6	-	23	-	5	100
F7	60	-	-	2	27	-	5	100
F8	60	-	-	4	25	-	5	100
F9	60	-	-	6	23	-	5	100
F10	60	2	-	-	-	27	5	100
F11	60	4	-	-	-	25	5	100
F12	60	6	-	-	-	23	5	100
F13	60	-	2	-	-	27	5	100
F14	60	-	4	-	-	25	5	100
F15	60	-	6	-	-	23	5	100
F16	60	-	-	2	-	27	5	100
F17	60	-	-	4	-	25	5	100
F18	60	-	-	6	-	23	5	100

Note: All formulations contain 2% (2mg) Talc and 2% (2mg) magnesium stearate, 2% (2mg) sodium saccharin ,SD= solid dispersion , CP= cross povidone, MCC =micro crystalline cellulose

EVALUATION OF TABLETS[17, 18, 19]

To design tablets and later monitor tablet production quality, quantitative evaluation and assessment of tablet chemical, physical and bioavailability properties must be made. The important parameters in the evaluation of tablets can be divided into physical and chemical parameters.

Physical appearance[20]

The general appearance of tablets, its visual identity and overall elegance is essential for consumer acceptance. The control of general appearance of tablet involves measurement of number of attributes such as tablet size, shape, colour, presence or absence of odour, taste, surface texture and consistency of any identification marks.

Tablet size and Thickness[21]

Control of physical dimensions of the tablets such as size and thickness are essential for consumer acceptance and tablet-tablet uniformity. The diameter size and punch size of tablets depends on the die and punches selected for making the tablets. The thickness of tablet is measured by Vernier calipers scale. The thickness of the tablet is related to the tablet hardness and can be used an initial control parameter. Tablet thickness should be controlled within ±5%. In addition, thickness must be controlled to facilitate packaging.

Average weight of Tablets[22]

Take randomly 20 tablets and weigh accurately 20 tablets and calculate the average weight.

Average weight = weight of 20 tablets /20

Weight variation test[23]

It is desirable that all the tablets of a particular batch should be uniform in weight. If any weight variation is there, that should fall within the prescribed limits:

±10% for tablets weighing 130mg or less

±7.5% for tablets weighing 130mg-324mg

±5% for tablets weighing more than 324mg. The test is considered correct if not more than two tablets fall outside this range.

When 20 tablets are taken for the test and not more than 1 tablet fall outside this range when only 10 tablets are taken for the test. The difference of weight in tablets can lead to variation in doses. For carrying out this test 20 tablets at random are taken and weighed. The weights of individual tablets are then compared to be equal to average weight.

Friability[24]

This test is performed to evaluate the ability of tablets to withstand abrasion in packing, handling and transporting. Friability of the tablet determined using Roche friabiltor. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25rpm and dropping a tablet at l height of 6 inches in each revolution. Preweighed sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were de-dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$F = \frac{W\text{initial} - W\text{final}}{W\text{initial}} \times 100$$

Hardness test[25]

This is to force required to break a tablet in a diametric compression. A tablet requires a certain amount of mechanical strength to withstand the shocks of handling in its manufacturing, packing, shipping and dispensing. Hardness of the tablet is determined by Stock's Monsanto hardness tester which consists of a barrel with a compressible spring. The pointer moves along the gauze in the barrel fracture.

***In-vitro* disintegration time**[26]

Disintegration time was determined using USP tablet disintegration apparatus (ED2L Electro lab, India) using 900 ml distilled water at room temperature. A tablet was placed in each of the six tubes of the apparatus. The time taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

Wetting time[27]

A piece of tissue paper folded double was placed in a Petri plate (internal diameter is 6.5 cm) containing 6 mL of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in minutes.

Water absorption ratio

A piece of tissue paper folded twice was placed in a small Petridis containing 6 ml of distilled water. A tablet was put on the paper and the time required for complete wetting of the tablet was measured. The wetting tablet was then weighed. Water absorption ratio "R" was determined using the equation as follows :

$$R = \frac{Wa - Wb}{Wb} \times 100$$

Where, Wa is Weight of tablet after water absorption and Wb is Weight of tablet before water absorption.

Drug content[28]

Drug content was determined by accurately weighing 5 tablets and crushing them in a mortar with the help of pestle. Then an accurately weighed quantity powder equivalent to 15mg of drug was transferred to a 10ml volumetric flask and the volume was made up to the mark with methanol and shaken.1 ml of the filtrate was diluted to 10ml with methanol. The absorbance of the resulting solution was recorded at 269nm. Content uniformity was calculated using formula.

$$\%Purity = 10\ C\ (Au/As)$$

Where, C= concentration, Au and As are absorbances obtained from standard preparation and assay preparation respectively.

***In-vitro* dissolution studies** [29]

In vitro drug release studies of all the formulations were carried out using tablet dissolution test apparatus (USP type II) at 50 rpm. Phosphate buffer pH6.8 was used as the dissolution media with temperature maintained at (37.0±0.5).An aliquot (5ml) sample was withdrawn at specific time intervals (5,10,15,30,45,60 minutes) and replaced with fresh medium to maintain a constant volume. The samples were filtered and analyzed by UV spectrophotometer at 269nm. The concentration was calculated using standard calibration curve.

RESULTS & DISCUSSION

PREFORMULATION STUDIES:-

Loratadine Hydrochloride Preformulation studies

S.NO	PARAMETERS	REPORT
1	Physical appearance	white or off–white crystals or powder
2	Solubility	Practically insoluble in water, soluble in acetone, dichloromethane, methanol and ethanol.
3	Melting point	132-135^{o}C

Determination of solubility

Solubility of Loratadine hydrochloride in various aqueous buffers

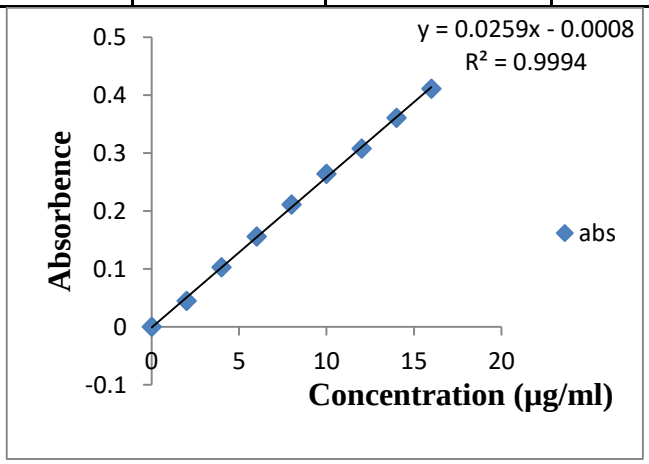
S. No	Solvent used	Solubility (mg/ml)
1	Distilled water	0.008
2	0.1 N HCl	4.9
3	0.1 N NaOH	9.2
4	6.8pH phosphate buffer	0.012
5	7.4pH phosphate buffer	0.009
6	4.5pH phosphate buffer	1.8

Linearity plot of Loratadine Hydrochloride in different solutions:

Standard solutions of Loratadine Hydrochloride were prepared in different solutions and absorption values were recorded at 245nm against distilled water, 0.1N HCl, 0.1N NaOH,4.5 pH acetate buffer, 6.8pH phosphate buffer and 7.4pH phosphate buffers as a blank. From this data, the standard curves of Loratadine hydrochloride were obtained.

Standard Graph of Loratadine Hydrochloride in Distilled water at 245nm

Concentration (µg/ml)	Absorbance	Concentration (µg/ml)	Absorbance
0	0	8	0.211
2	0.045	10	0.264
4	0.103	12	0.308
6	0.156	14	0.361

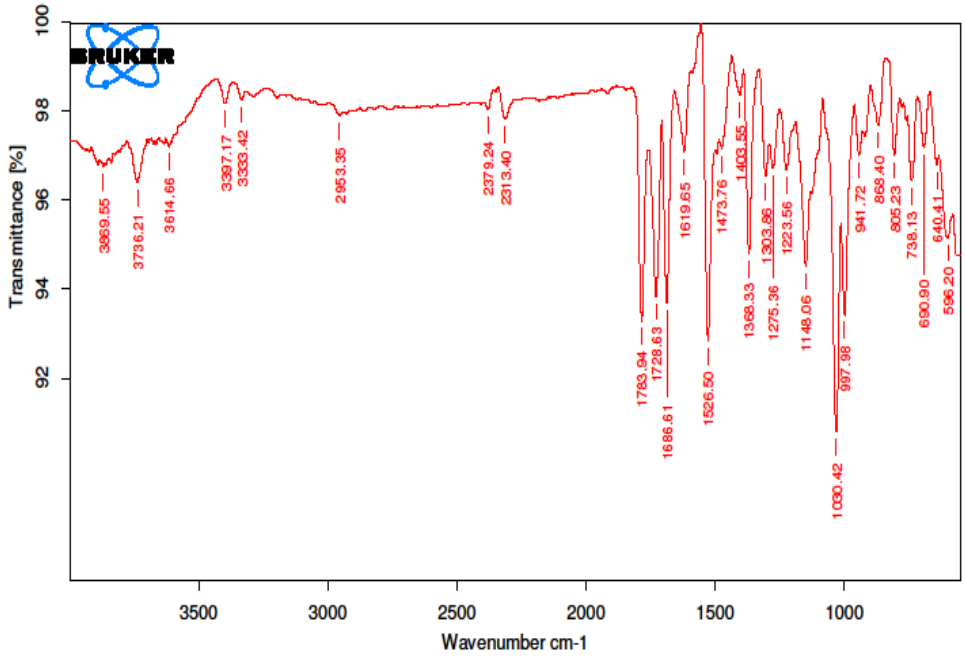


Calibration curve of Loratadine Hydrochloride in Distilled water

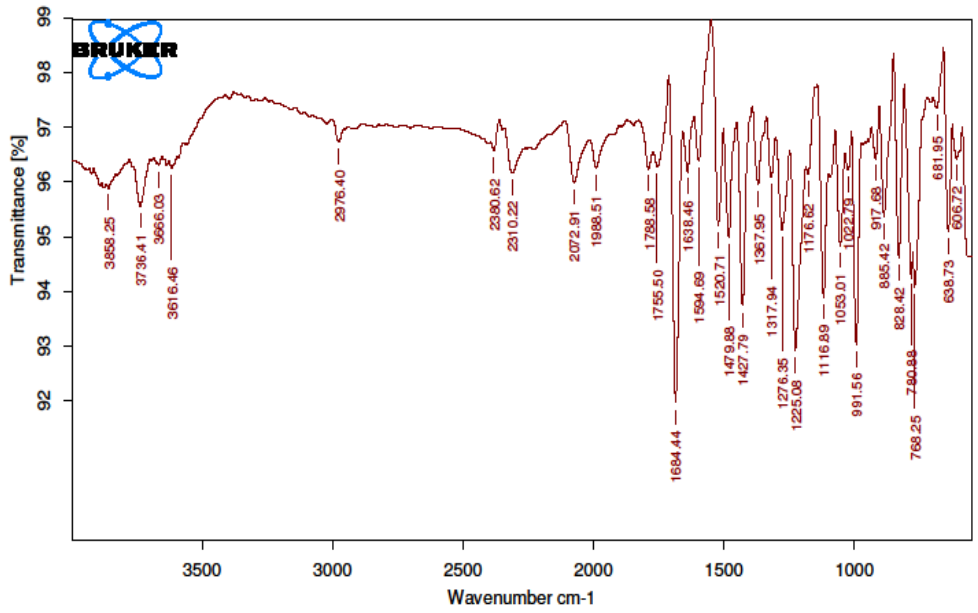
Characterization of drug and polymers

Fourier transform infra-red spectroscopy (FTIR)

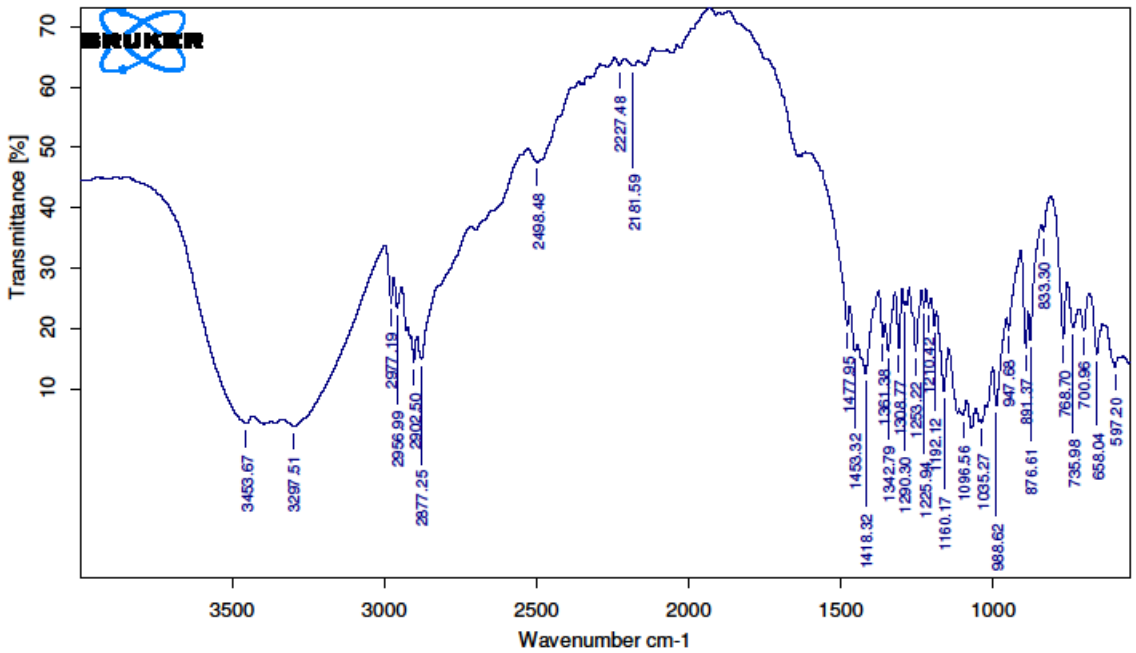
FTIR spectra of optimized formulation show bands for specific functional group in Loratadine hydrochloride, cross povidone and urea. Spectrum illustrates bands for Loratadine hydrochloride at wave number 1763.84 cm^{-1} (C=O), 2953.35 cm^{-1} (aromatic C-H stretching), 1223.58 cm^{-1} (C–O stretching), 1619.95 cm^{-1} (C=C stretching) .Cross povidone contain functional groups shows bands at wave number 1818.93 cm^{-1} (carbonyl group), 1342.50 cm^{-1}(C–N stretching), 3026.41 cm^{-1} (C–H stretching). Urea shows bands at 1640.38 cm-1 (C=O stretching), 2852.86 (C–H stretching). There were no significant interactions observed between the drug and excipients as per the FT IR studies.



FTIR spectrum of optimized formulation



FTIR spectrum of Loratadine hydrochloride



FTIR spectrum of Lactose anhydrous

Preparation of solid dispersions

Solubility improvement was observed with solid dispersion preparations compared to pure drug this increase solubility due to in the concentration of carriers possibly due to the increased wettability of the drug by the carrier, drug particle size reduction in the course of the solid dispersion preparation, polymorphic transformation of drug crystals and chemical interactions between drug and carrier. Fusion method with urea as carrier, the solubility of drug was high for 1:5 ratio when compared with other ratios and for PEG 6000 as carrier, the solubility of drug was high for 1:6 ratio as compared to other ratios. Among all the ratios drug: urea in 1:5 improved the water solubility of the drug by 9 folds when compared with other methods.

Preparation of solid dispersions by fusion method

Carrier	Drug: Carrier ratio	Solubility (mg/ml)
		Fusion Method
Urea	1:1	0.018
	1:2	0.032
	1:3	0.048
	1:4	0.061
	1:5	0.072
	1:6	0.067
PEG 6000	1:1	0.012
	1:2	0.021
	1:3	0.03
	1:4	0.041
	1:5	0.053
	1:6	0.065

Preformulation characteristics of Loratadine hydrochloride ODTs prepared by solid dispersion method.

Tableting characteristics of Loratadine hydrochloride ODTs prepared by solid dispersion method.

Formulation	Weight (mg)	Drug content (%)	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)
F1	99.37±0.81	98.76±0.47	2.9±0.06	0.59	3.84±0.032
F2	98.94±1.26	99.45±0.65	3.0±0.06	0.46	3.85±0.028
F3	99.46±1.09	99.11±0.52	2.9±0.08	0.50	3.86±0.024
F4	99.7 ±1.68	99.23±0.60	2.9±0.09	0.48	3.86±0.051
F5	99.02±1.32	99.28±0.4	3.0±0.06	0.55	3.88±0.048
F6	99.02±1.32	98.96±0.58	3.0±0.18	0.48	3.90±0.052
F7	99.3 ±1.49	99.31±0.24	2.9±0.11	0.53	3.92±0.038
F8	99.01±1.92	98.86±0.28	3.0±0.07	0.58	3.91±0.042
F9	99.43±1.55	99.35±0.38	3.0±0.13	0.6	3.90±0.040
F10	99.6±0.81	98.76±0.49	2.9±0.08	0.51	3.86±0.034
F11	99.8±1.45	98.81±0.60	3.0±0.19	0.43	3.86±0.023
F12	100.1±0.88	98.98±0.56	3.0±0.14	0.54	3.87±0.044
F13	99.8 ±1.04	99.33±0.58	2.9±0.12	0.51	3.89±0.051
F14	99.9 ±1.24	98.85±0.69	3.0±0.05	0.46	3.85±0.029
F15	99.3 ±1.54	98.76±0.56	3.0±0.07	0.53	3.88±0.046
F16	99.6 ±1.70	99.08±0.29	3.1±0.06	0.58	3.86±0.025
F17	98.8 ±1.44	98.86±0.39	2.9±0.07	0.57	3.84±0.034
F18	99.7 ±1.05	99.63±0.45	3.0±0.06	0.64	3.87±0.031

Tableting characteristics of Loratadine hydrochloride ODTs prepared by solid dispersion method

Formulation	Bulk density (g/cc)	Tapped density (g/cc)	Hausner ratio	Compressibilty index (%)	Angle of repose (ɵ)
F1	0.370	0.414	1.11	10.8	30.64
F2	0.360	0.405	1.13	11.26	29.32
F3	0.384	0.43	1.19	10.69	29.52
F4	0.380	0.425	1.11	10.58	31.23
F5	0.366	0.4	1.09	8.5	30.56
F6	0.388	0.429	1.10	9.6	32.04
F7	0.360	0.404	1.12	10.89	31.76
F8	0.366	0.412	1.08	11.16	29.54
F9	0.380	0.432	1.12	12.03	29..67
F10	0.377	0.423	1.12	11.04	31.85
F11	0.357	0.388	1.13	7.98	29.67
F12	0.380	0.430	1.13	11.6	32.54
F13	0.366	0.404	1.10	9.4	31.05
F14	0.363	0.412	1.13	11.89	30.36
F15	0.377	0.421	1.11	10.45	30.64
F16	0.373	0.416	1.11	10.3	31.78
F17	0.370	0.408	1.10	9.31	29.08
F18	0.384	0.434	1.13	11.5	32.67

The result of the uniformity of weight, hardness, thickness, friability and drug content of the tablet were given in table. All the tablets from F_1 to F_{18} formulation complied with the official requirements of the uniformity of weight.

Friability of all the formulations was ranged from 0.43% to 0.64%.

The thickness of all the formulations was ranged from 3.8±0.032to 3.92±0.038.

The hardness of all the formulations was ranged from 2.9±0.06 Kg/cm2 to 3.1±0.08 Kg/cm^2.

All the fast dissolving formulations shown good uniformity in drug content and they contain 98.76±0.47% to 99.63±0.45%w/w of loratadine hydrochloride.

The disintegration time, wetting time and water absorption ratio of the prepared formulations was determined. Among three different concentrations of super disintegrates the cross-povidone was optimized at 6% showed better disintegration time compared to sodium starch glycolate and croscarmellose sodium. This may be due to wicking nature of cross-povidone when compared to sodium starch glycolate and croscarmellose sodium as it swells and

disintegrates the tablet. The study involves screening the synergistic effect of diluent and disintegrate on disintegration time by taking avicel and lactose as different diluents. Formulation containing cross povidone with lactose which showed the less disintegration time of 10 sec which can be proved by its wetting time and water absorption ratio results

***In-vitro* dissolution studies**

The *in-vitro* release profile of fast dissolving tablets of Loratadine hydrochloride were conducted in 6.8 pH phosphate buffer for all formulations.

Among formulations containing cross-povidone with different diluents, F15 (cross-povidone with lactose) showed high drug release of 99.55% at 20min. Among formulations containing sodium starch glycolate with different diluents, F18 (sodium starch glycolate with lactose) showed high drug release of 99.68% at 25min. Among formulations containing croscarmellose sodium with different diluents, F17 (croscarmellose sodium with lactose) showed high drug release of 99.72% at 30min.

From the results it was observed that among all the formulations of cross-povidone, formulation with lactose as diluent (F_{15}) showed the highest drug release of 99.55% at 20 min compared to avicel. This may be due to more soluble nature of lactose which makes it dissolve the drug in the medium at faster rate compared to avicel which swells to more extent and has little water uptake.

Formulations containing cross povidone showed the highest drug release than formulations containing sodium starch glycolate and croscarmellose sodium. This may be due to cross povidones porous morphology enables them to rapidly absorb liquids into the tablet by capillary action and pronounced hydration capacity that results in faster disintegration and dissolution.

DISSOLUTION PROFILE

In-vitro drug release profile of Loratadine hydrochloride for formulations F_1 to F_6

Cumulative percent (±S.D.) drug release						
Time (min)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
5	20.71±0.47	28.54±0.37	31.52±0.33	28.36±0.51	36.87±0.36	43.12±0.46
10	31.67±0.48	36.72±0.51	45.42±0.42	36.72±0.44	50.29±0.43	62.48±0.48
15	44.9±0.35	50.81±0.33	67.35±0.48	47.16±0.36	63.17±0.47	79.84±0.37
20	52.9±0.42	62.82±0.38	78.14±0.36	61.78±0.42	77.44±0.35	98.89±0.41
25	68.04±0.45	80.92±0.41	98.85±0.39	78.14±0.5	98.5±0.39	
30	82.66±0.38	98.45±0.52		98.85±0.41		
40	99.18±0.41					

Plots of cumulative percentage drug release versus time for Formulations from F_4 to F_6

In-vitro drug release profile of Loratadine hydrochloride for Formulations F_7 to F_{12}

Cumulative percent (±S.D.) drug release						
Time (min)	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
5	10.87±0.38	17.52±0.36	22.45±0.72	20.88±0.46	31.1±0.34	38.33±0.38
10	18.92±0.41	28.71±0.41	35.67±0.34	29.54±0.37	40.2±0.45	52.03±0.42
15	29.23±0.45	36.72±0.47	51.86±0.44	38.72±0.51	51.86±0.48	64.39±0.45
20	39.15±0.48	49.25±0.36	64.22±0.47	56.81±0.33	66.3±0.39	79.18±0.37
25	51.51±0.53	64.04±0.44	82.32±0.39	67.82±0.38	81.62±0.35	99.68±0.51
30	66.83±0.36	79.88±0.39	98.67±0.45	81.92±0.41	99.89±0.44	
40	79.88±0.45	99.15±0.35		99.76±0.52		
50	98.5±0.36					

In-vitro drug release profile of Loratadine hydrochloride for Formulations F_{13} to F_{18}

Cumulative percent (±S.D.) drug release						
Time (min)	**F13**	**F14**	**F15**	**F16**	**F17**	**F18**
5	30.1±0.48	38.56±0.32	46.84±0.39	13.22±0.42	19.88±0.46	21.23±0.26
10	37.41±0.45	51.41±0.36	67.35±0.41	20.18±0.56	28.54±0.37	34.45±0.38
15	52.03±0.36	65.53±0.39	81.45±0.36	32.89±0.48	36.72±0.51	47.16±0.41
20	65.43±0.39	83.61±0.44	99.55±0.42	46.12±0.34	50.81±0.33	67.7±0.36
25	83.71±0.41	99.78±0.47		54.64±0.42	62.82±0.38	81.27±0.48
30	99.72±0.38			68.39±0.51	80.92±0.41	99.72±0.39
40				81.45±0.38	99.65±0.52	
50				99.89±0.31		

SUMMARY

Oral disintegrating tablets of Loratadine hydrochloride using solid dispersion were prepared to enhance solubility and dissolution rate in order to have immediate action and to increase patient compliance and convenience. Loratadine hydrochloride is a class of azatadine class of antihistamic drug which belongs to BCS-II having low solubility and high permeability. One of the major problems with this drug is its low solubility in biological fluids, which results in poor bioavailability after oral administration. The solubility of poorly soluble drug was enhanced by preparing solid dispersions of the drug.

Solid dispersions of the drug were prepared by fusion method using two hydrophilic carriers PEG 6000 and urea respectively. Different ratios of drug: carrier was taken 1:1,1:2,1:3,1:4 and 1:5. Enhanced drug solubility was observed by increasing the concentration of carrier. Among all the ratios drug: urea in 1:5 prepared by fusion method was optimized which improved the water solubility of the drug by 9 folds when compared with other ratios. Different formulations were prepared with varying concentration of super disintegrates with different diluents. Formulations were screened based on disintegration time and for the best selected formulations combination of diluents were used and compressed into oral disintegrating tablets. Among three different concentrations of super disintegrates the cross-povidone was optimized at 6%. Cross povidone showed better disintegration time compared to other super disintegrates. This may be due to wicking nature of cross-povidone.

Among all the formulations, F_{15} formulation containing 6% cross-povidone as super disintegrate and lactose as diluents showed the least disintegration time of 10 seconds and highest drug release of 99.55% at 20 minutes. This may be due to more soluble nature of lactose which makes it dissolve the drug in the medium at faster rate compared to avicel which swells to more extent and has little water uptake.

CONCLUSION

The present study proved the successful preparation of fast dissolving tablets of Loratadine hydrochloride by using solid dispersions of drug with super disintegrates. Significant improvement in solubility of drug was observed with prepared solid dispersions. Cross povidone was optimized at 6% concentration based on *in-vitro* disintegration time. Among all the formulations F_{15} formulation (lactose with cross-povidone as super disintegrate) showed the less disintegration time of 10 seconds and highest drug release of 99.55% at 20 minutes. Hence it can be concluded that using of super disintegrates would be quite effective in providing fast onset of action without the need of water for swallowing.

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