Formulation and Evaluation of Chewable Tablets of Loratadine Prepared By Aqueous and Non-Aqueous Techniques

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Abstract

Aim of present study was to formulate Loratadine chewable tablets by using aqueous and nonaqueous technique and different super disintegrants and evaluating its characteristics. The chewable tablets of Loratadine were prepared with different level addition of super disintegrants; sodium starch glycollate, crosspovidone and Croscarmellose sodium, for each designed formulations, powder mixed blend of drug and excipients was prepared and evaluated for various parameters. Melting range of Loratadine sample was found to be 135.00 ± 1^{O}C. pH of Loratadine was found around 7.4 indicating weakly basic in nature. The logP value of Loratadine was found to be in the range of 2.5 to 4 indicating the lipophilic nature of drug. UV absorption spectrum of Loratadine in 0.1 N HCl shows λmax at 247.5 nm. DSC thermogram showed that there was no major difference in onset temperature, end set temperature and peak temperature when compared Chapter-8 Result and Discussion Shri Bherulal Pharmacy Institute, Indore PAGE 57 with pure drug thermogram. All the formulations showed similar thickness. Moreover, friability, hardness, weight variation of all the trials were found to be within the official limits. The assay of drug was performed using UV-Spectrophotometer at wavelength 280nm, using 0.1N HCl as blank solution. All the formulations were within the specification (95-105%) as per USP. The F8 is considered as more optimized formulation. Stability studies of formulation F8 were carried out by placing the samples at temperature 40 ^{O}C and different relative humidity conditions 75% RH. From the above observations it was found that there were no significant changes in disintegrate time, release characteristics and physicochemical properties of the tablets used in release study.

Keywords: **Loratadine, super disintegrants; sodium starch glycollate, crosspovidone and Croscarmellose sodium**

Introduction:

Loratadine act as an anti-histaminic and used as potential drug to get the quick relief in suddenly arising allergic reactions like urticaria, angeoedema, in treatment of perennial and seasonal allergic rhinitis, considering this parameter there is a need formulate the Loratadine as fast disintegrating Chewable Tablets[1]. Present Chewable Tablets by passes the hepatic metabolism unlikely of the other conventional oral dosage forms which are relatively less bioavailable[2]. This Chewable Tablets gives absorption of drug from oral cavity, pharynx and oesophagus; results in quick onset of action, improved bioavailability and patient compliance[3].

Tablet defined as solid dosage forms containing drug substances with or without suitable diluents and prepared either by compression or molding method[4]. Tablets are solid dosage forms each containing a unit dose of one or more medicaments[5]. Chewable tablets are intended to disintegrate smoothly in mouth at a moderate rate either with or without actual chewing, characteristically chewable tablets have a smooth texture upon disintegration, are pleasant tasting and leave no bitter or unpleasant taste[6]. Chewable tablets are intended to be chewed in the mouth prior to swallowing and are not expected to be swallowed intact[7]. The

purpose of chewable tablet is to provide a unit dosage form of medication which can easily be administered to children or to the elderly who may have difficulty in swallowing a tablet intact[8]. Almost invariably, the formulation problem involves at least one of the following: undesirable taste, bad mouth-feel, or aftertaste. The desired product should prevent or minimize stimulation of the taste buds, contain a suitable flavor and sweetener, and achieve good mouth-feel and compressibility[9].

Aim of present study is to formulate Loratadine chewable tablets by using aqueous and nonaqueous technique and different super disintegrants and evaluating its characteristics.

Materials and Method:

Drug sample Loratadine was obtained as a gift sample from Cipla, Pithampur and Hetero Drugs, Hyderabad respectively. Polyvinyl pyrolidone-K30, Aspartam were purchased from Himedia. All other solvent were belongs to L.R. grade.

Method of Formulation and characterization of powder blend: Accurate quantity of drug and all ingredients were weighed according to formula shown in Table and powder except aerosil and magnesium stearate was blended homogeneously in mortor and pestel for 15 minutes. Prepared powder blend was passed through sieve No.#60. Finally aerosil and magnesium sterate passed through sieve No. #30 was added and further mixed for10 minutes. Powder blend was evaluated for angle of repose, bulk density, Tapped density, Compressibility Index and Hausner ratio.

Preparation of chewable tablets: Chewable tablets of Loratadine were prepared by using aqueous granulation and non-aqueous granulation method.

Table No. 1: Formulation of Chewable Tablet of Loratadine

Chemical Name	Batches Numbers							
	T1	T2	T3	T4	T5	T6	T7	T8
Loratadine	10	10	10	10	10	10	10	10
Lactose	157	155	150	146	154	147	140	135
Mannitol	-	-	12	12	-	-	20	20
Aspartame	11	12	-	-	15	15	-	-
Avicel 101	10	12	15	17	10	15	17	20
PVP	5.5	4.85	5	5	5	5.45	5	5.5
Talc	3.5	3	3	3.85	3	3.4	3	3.35
Sodium starch glycollate	1	2	3	4	-	-	-	-
Crosscarmellose sodium	-	-	-	-	1	2	3	4
Magnesium Stearate	2	2	2	2	2	2	2	2
IPA	-	0.15ml	-	0.15ml	-	0.15ml	-	0.15ml
Distilled Water	q.s		q.s		q.s		q.s	
Total	200	200	200	200	200	200	200	200

Aqueous Method: In this method, active ingredient i.e. Loratadine was mixed with lactose, avicel 101 and mannitol. Add 10ml of 10% PVP and mix, until wet damp mass was formed. Then passed damp mass from sieve no.12 and granules were formed. Dry these granules in oven at 50˚C for 30 minutes. Then mix it with sweetening agent (Mannitol or Aspartame), flavoring agent, coloring agent, magnesium stearate and talc. Tablets were formed by using single punch machine equipped with 15mm punch and die.

Non-Aqueous Method: In this method, active ingredient i.e. Loratadine was mixed with lactose, avicel 101 and mannitol. Add 10%PVP in isopropyl alcohol solution and formed granules. Dried these granules in hot air oven at 40-50˚C. Then again pass these granules from sieve No. 22. After this, mix it with sweetening agent (Mannitol or Aspartame), flavoring agent, coloring agent, magnesium stearate and talc. Then this mixture was tested for evaluation of the flow properties and made tablets by using single punch machine.

Result and Discussion:

Preformulation parameters: In the present study, an attempt was made to formulate nine formulations of the chewable tablets of Loratadine were prepared with different level addition of super disintegrants; sodium starch glycollate, crosspovidone and Croscarmellose sodium, For each designed formulations, powder mixed blend of drug and excipients was prepared and evaluated for various parameters as follows:

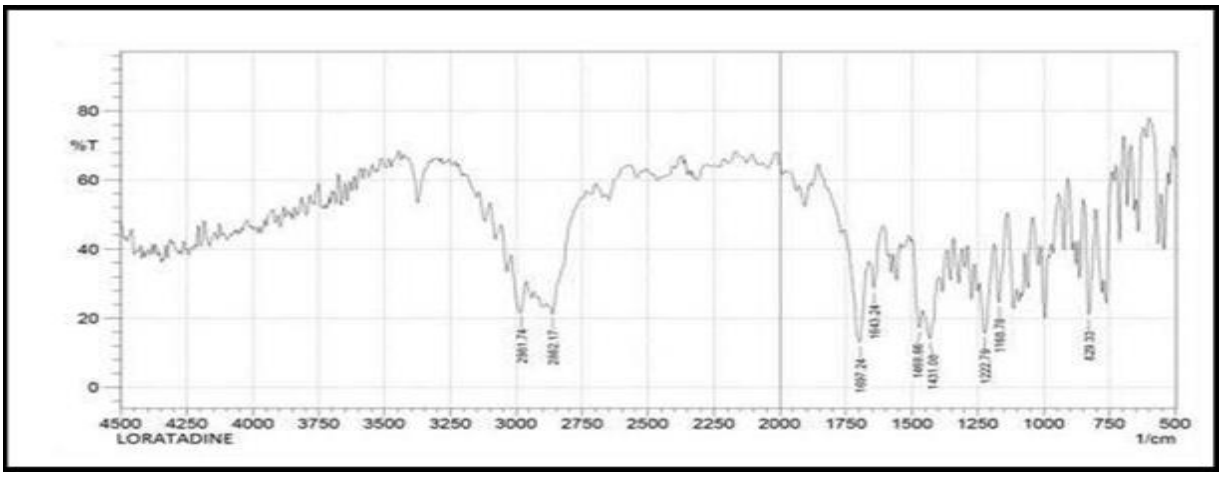

Figure 1: FT-IR of pure drug Loratadine

Table No. 2: Characteristic frequencies (Interpretation) in IR spectrum of Loratadine

Wave No.(cm^{-1})	Inference
2981.74	C-H stretching of aromatics
1643.24	C=O stretching
829.33	C-Cl stretching
1465.66	C=N stretching of pyridine
1431	C-C skeletal stretching
875	Cl stretching
1365	C-N stretching of tertiary amine

Physicochemical parameters of drug

Loratadine sample was white, fine powder having no odor and taste. Melting range of Loratadine sample was found to be 135.00 ± 10C. The reported melting point range for Loratadine is 134 to 136ºC. Hence, experimental values are in good agreement with official values. pH of Loratadine was found around 8.1 indicating weakly basic in nature. Log-p value of Loratadine was found to be in range of 2.5 to 4 indicating the lipophilic nature of drug and value was disclosed in table.

Table No. 3: Partition Coefficient Value of Loratadine

Drug	Observed	Reference
Loratadine	3.9	3.83 -3.98

Solubility study of the drug

Table No. 4: The solubility of Loratadine in different solvents

S. No.	Solvent	Result
1.	Distilled water	Practically insoluble
2.	Methanol	Freely soluble
3.	Chloroform	Freely Soluble
4.	Acetone	Freely Soluble
5.	0.1 N NaOH	Freely Soluble
6.	Toluene	Freely Soluble

Analytical Method:

Determination of λmax and Preparation of Calibration Curve of Loratadine by using 0.1 N HCl

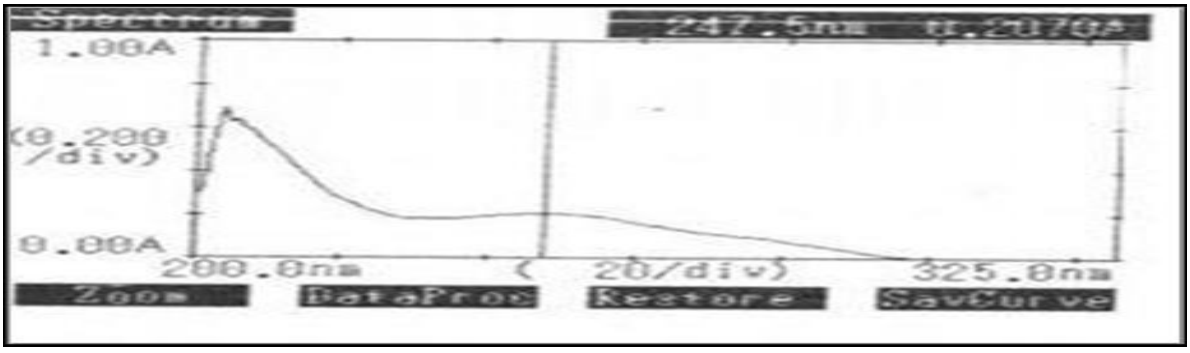

Figure 2: UV Spectra of Loratadine in 0.1 N HCL

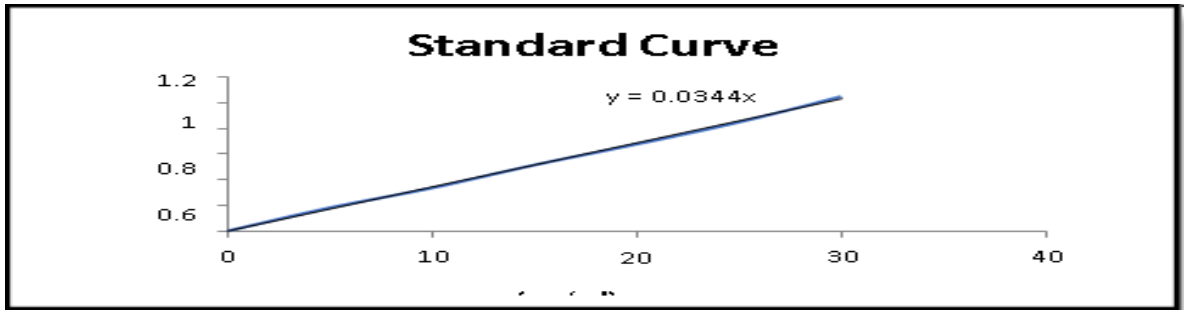

Figure 3: Calibration curve for Loratadine in 0.1 N HCl

Determination of λmax and preparation of calibration curve of Loratadine by using phosphate buffer pH 6.8

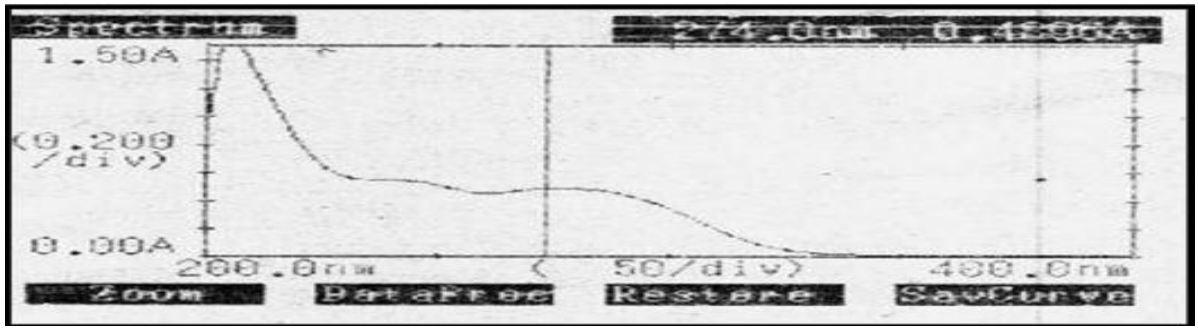

Figure 4: UV spectra of Loratadine in Phosphate buffer pH 6.8

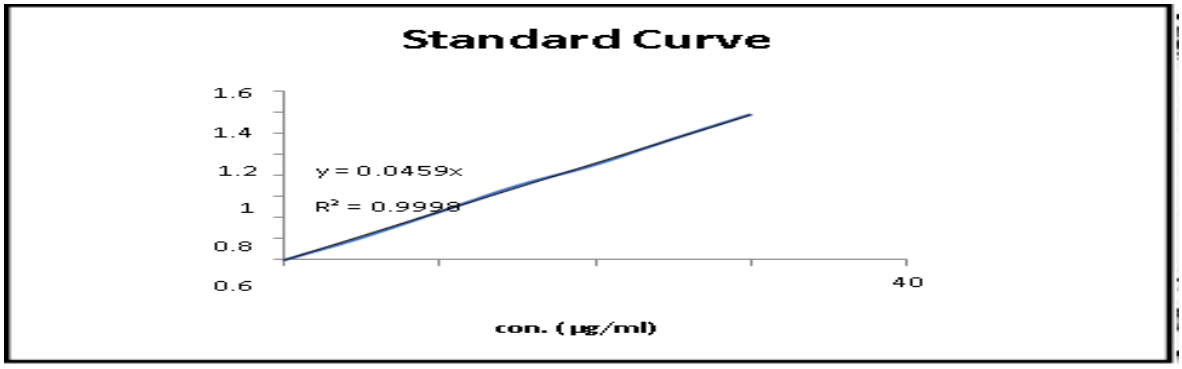

Figure 5: Calibration curve for Loratadine in Phosphate buffer pH 6.8

Drug –polymere compatibility study

Fourier Transform Infra-Red Spectroscopy (FT-IR)

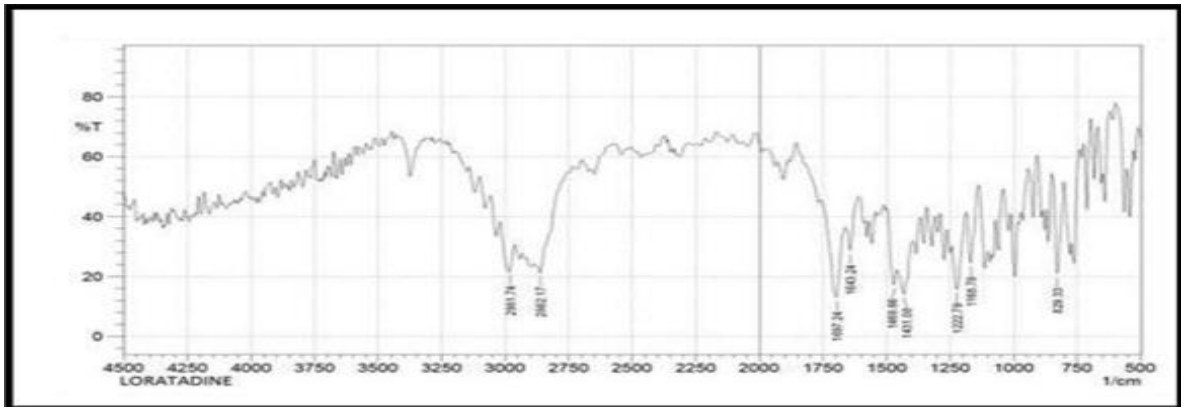

Figure 6: FTIR spectrum of Loratadine

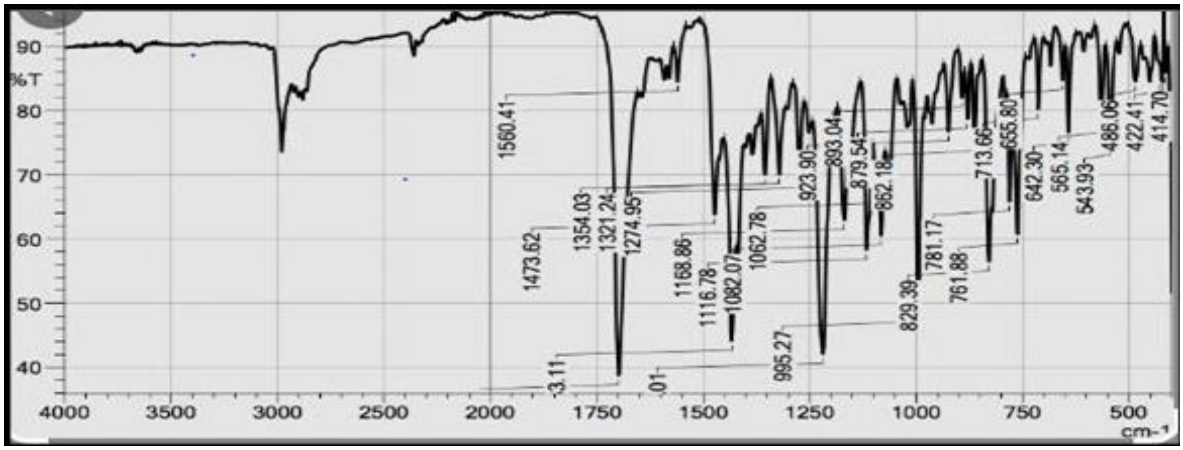

Figure 7 Drug and super disintegrant compatibility studies

Drug-excipient mixture does not produce any significant changes in organoleptic property, bulk density, true density, compressibility index, angle of repose and drug content. The compatibility between the drug and the selected super disintegrants were evaluated using FTIR peak matching method. From above interpretation table it was concluded that, there was no appearance or disappearance of the principal peaks in the super disintegrants drug mixture, which confirmed the absence of any chemical incompatibility between the drug and the super disintegrants.

Differential scanning calorimetry

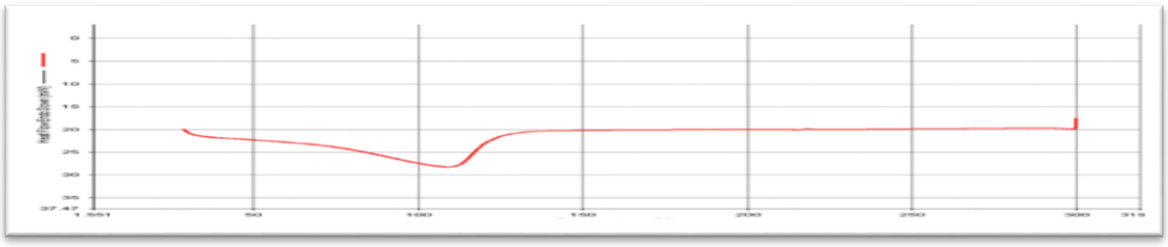

Figure 8: DSC thermogram of Loratadine

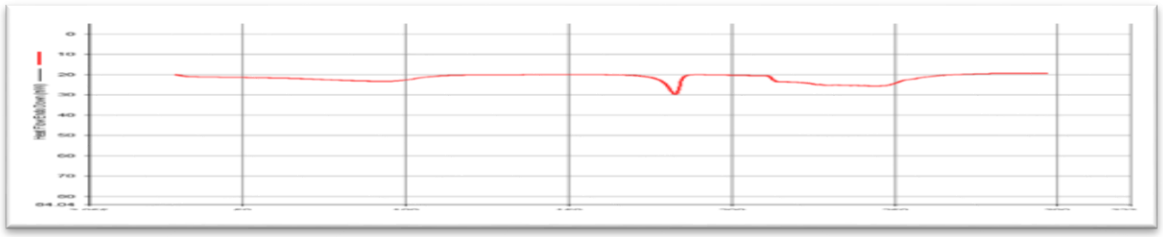

Figure 9: DSC thermogram of physical mixture

According to Figures 8.12 to 8.15 and Table 8.12, DSC thermogram showed that there was no major difference in onset temperature, end set temperature and peak temperature when compared with pure drug thermogram. Therefore, it could indicate that there was no incompatibility between drug and different polymers.

Evaluation of Powder Blends of Loratadine

Table No. 5: Determination of flow properties of liquisolid powder

Batch No.	Bulk Density (g/ml)	Tapped Density (g/ml)	Hausner's Ratio	Carr's Index (%)	Angle of repose (ɵ)
F1	0.356	0.438	1.13	12.11	25o.21
F2	0.385	0.438	1.11	11.65	24o.80
F3	0.362	0.428	1.14	11.14	26o.28
F4	0.372	0.425	1.16	12.64	21o.34
F5	0.389	0.417	1.15	13.26	27o.35
F6	0.368	0.404	1.17	14.41	26o.14
F7	0.387	0.436	1.11	14.13	28o.49
F8	0.349	0.446	1.18	12.35	29o.31

Table No. 6: Characterization of tablets of all formulations

S. No	Formulation Code	Hardness (kg/cm2)	Friability (%)	Weight Variation (%)	Thickness (mm)	Drug Content (%w/w)
1	F1	3.22	0.8	95.5	2.81	98.60
2	F2	2.85	0.7	97.4	2.7	98.64
3	F3	3.12	0.9	95.7	2.90	95.24
4	F4	3.5	0.8	96.45	2.72	98.70
5	F5	4.0	0.7	96.50	2.80	97.60
6	F6	3.6	0.8	98.12	2.9	97.74
7	F7	4.3	0.7	98.88	3.0	98.82
8	F8	3.0	0.8	98.95	3.1	98.86

All the formulations showed similar thickness. Moreover, friability, hardness, weight variation of all the trials were found to be within the official limits. The assay of drug was performed using UV-Spectrophotometer at wavelength 280nm, using 0.1N HCl as blank solution. All the formulations were within the specification (95-105%) as per USP. The F8 is considered as more optimized formulation as shown in the Table 5.

Table No. 7: Disintegration time

Formulations	Disintegrate time (sec) (Mean ± S.D. n = 3)
F1	35
F2	27
F3	30
F4	26
F5	31
F6	25
F7	21
F8	29

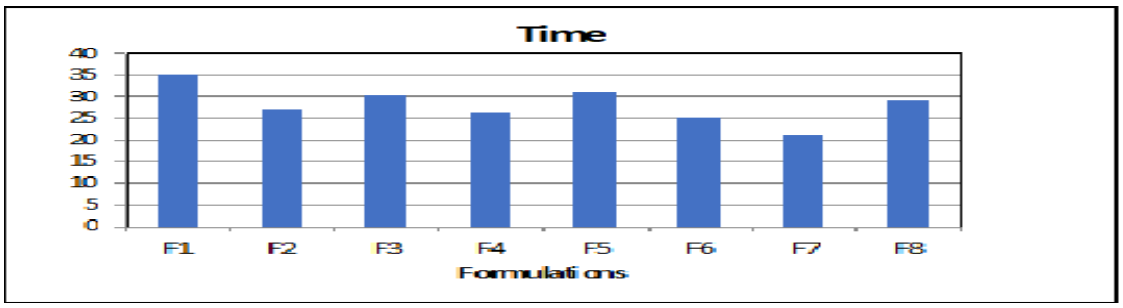

Figure 10: Disintegrate profile of Chewable Loratadine tablets (F1 – F8)

Wetting Time:

Wetting time was determined for all formulation. The value lies between 19.40 to 35.64 sec

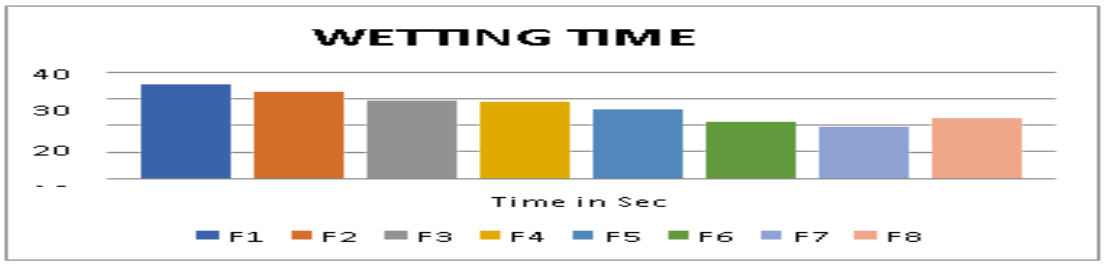

Figure 11: Wetting time

Water Absorption Ratio:

Water absorption ratio within obtained limit ranged found from 75.76 to 90.78

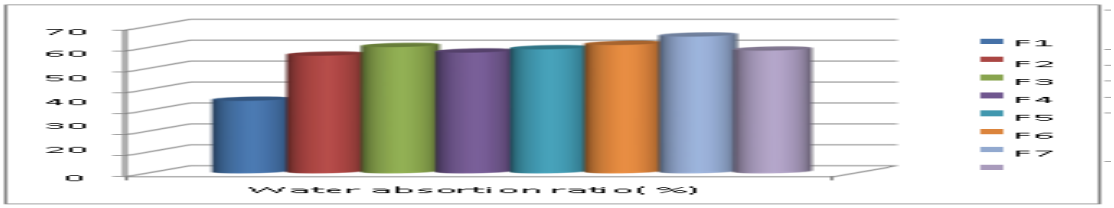

Figure 12: Water Absorption Ratio

Table No. 8: *In-Vitro* Drug Release Study

Formulation Code	% Cumulative release					
	5 min	10 min	15 min	20 min	25 min	30 min
F1	58.25	62.08	63.95	65.37	68.48	69.89
F2	59.24	65.6	68.66	69.29	71.18	73.19
F3	65.98	67.94	70.92	75.92	79.45	80.45
F4	69.19	72.94	78.71	80.8	82.27	83.67
F5	67.8	81.78	84.94	87.57	88.03	90.67
F6	77.45	82.47	89.63	92.28	93.85	94.89
F7	78.47	90.26	95.26	96.5	98.16	99.35
F8	76.98	85.41	86.93	88.93	93.04	98.61

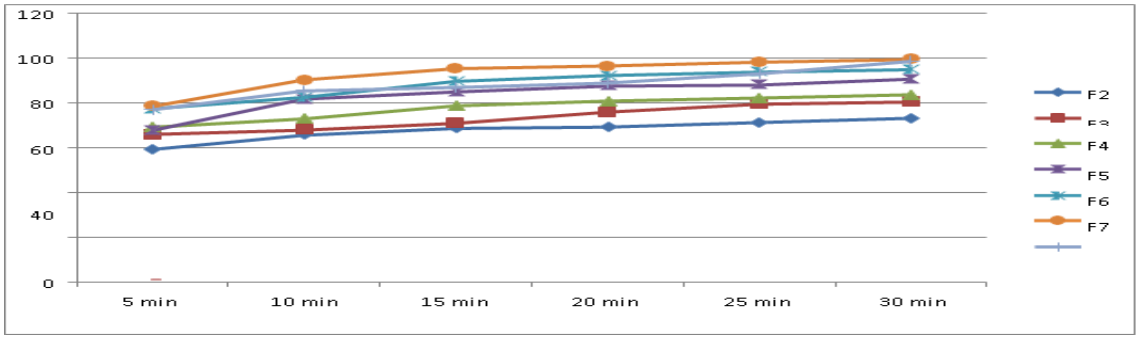

Figure 13: *In-Vitro* Drug Release Study

Best formulation drug release formulation F7 within limit 99.35% at completely time 30 minute.

Percentage Cumulative Drug Release For F10 and Marketed Formulation

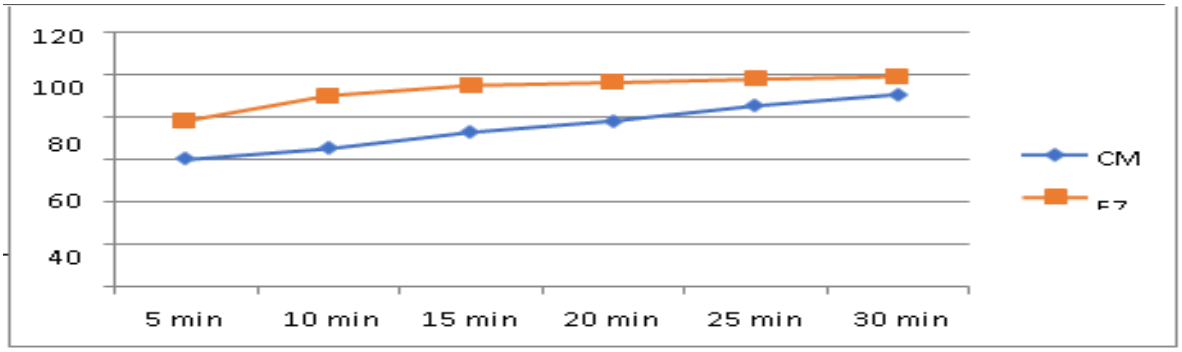

Figure 14: Comparison of best formulation and marketed formulation is depicted

Stability Studies

Table No. 9: Stability results (Initial to 3rd Month)

Evaluation Parameter	Formulation- F8 observations		
	Initial	After 15 days	After one month
Physical Appearance	White, round, flat tablet	No change	No change
Hardness (kg/cm2)	3.0	3.04	3.15
Disintegrate test (sec.)	21 sec	21.12	21.15
Dissolution test (%)	99.35	98.28	98.15
Drug content (% w/w)	98.86	98.75	98.15

Stability studies of formulation F8 were carried out by placing the samples at temperature 40oC and different relative humidity conditions 75% RH. From the above observations it was found that there were no significant changes in disintegrate time, release characteristics and physicochemical properties of tablets used in release study.

Conclusion:

The present investigation was undertaken to formulate and evaluate instant release chewable tablet of Loratadine with the main objective of quick onset of action followed by pleasant mouth feel and improved patient compliance. By using two different method like aqueous and non- aqueous method. In the modern era, chewable tablets are preferred over conventional dosage forms by pediatric, geriatric and bedridden patients due to difficulty in swallowing, lesser amount of water for swallowing medications as well as unable to tolerate the bitter taste of certain drugs. Chewable tablets of Desloratadine (DS) were formulated by aqueous and non-aqueous granulation method using water paste and Isopropyl alcohol (IPA) as a wetting agents respectively. Loratadine is used to treat the symptoms of allergy such as sneezing, watery eyes. In the recent research, we have formulated eight trials by various concentrations of excipients.

Conflicts of Interests:

There are no conflicts of interests.

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