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Formulation and Characterization of Fexofenadine hydrochloride Fast Dissolving Tablet by using various Superdisintegrants.

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Abstract

In the present work, fast dissolving tablets of fexofenadine HCl were designed with a view to enhance patient compliance by direct compression method. The present work studied the effect of superdisintegrants on release rate of fexofenadine HCl in the form of fast disintegrating tablet. For the present study range of superdisintegrants in their different concentrations, were used. The superdisintegrants used were crosscarmellose sodium, crosspovidone and kyron T-314. The blends were prepared by direct compression technique. The tablets were evaluated for hardness, thickness, friability, drug content, weight variation and in-vitro drug release studies in pH 6.8.

Keywords: Fexofenadine hydrochloride, fast dissolving tablets, crosscarmellose sodium, crospovidone, kyron T-314.

Introduction

Many patients have difficulty to swallow tablets and hard gelatin capsules and thus does not comply with prescription, which results in high incidence of non-compliance and ineffective therapy. It is estimated that 50% of the population is affected by this problem. Recent advances in Novel Drug Delivery Systems (NDDS) aim to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach is "Fast Dissolving Tablets (FDT) [1-5].

According to European Pharmacopoeia, the FDT should disperse/disintegrate in less than three minutes. The basic approach used in development of FDT is the use of superdisintegrants like cross linked carboxymelhylcellulose (croscarmellose), sodium starch glycolate (Primogel, Explotab), polyvinylpyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva. Their growing importance was underlined recently when European pharmacopoeia adopted the term "Orodispersible tablet" as a tablet that to be placed in the mouth where it disperses rapidly before swallowing. The bioavailability of some drugs may be increased due to absorption of drug in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. More ever, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablet. The technologies used for manufacturing fast-dissolving tablets are freeze-drying, spray-drying, tablet molding, sublimation, sugar-based excipients, tablet compression, and disintegration addition. As a result of increased life expectancy, the elderly constitute a large portion of the worldwide population today [6-7]. These people eventually will experience deterioration of their physiological and physical abilities. fexofenadine HCl is a non-sedating anti-histamine used in systemic relief of allergic conditions including seasonal allergic rhinitis and urticaria [8].

Fexofenadine HCl was preferred as a model drug for formulation development. fexofenadine HCl is biopharmaceutical classification system type II as it possesses low solubility and high permeability. This depicts its good bioavailability which in turn suggests its ideal candidature for fast disintegrating drug delivery system. It is indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults and children 2 years of age and older and for treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 months of age and older. These conditions are commonly found in pediatric patients, where palatability is of main concern. In case of conventional

tablets there is problem of swallowing of tablet particularly in pediatric patient.

In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration. Although superdisintegrants primarily affect the rate of disintegration, but when used at high levels they can also affect mouth feel, tablet hardness and friability [9].

In the present work an attempt was made to formulate fast disintegrating tablet of fexofenadine HCl which get disintegrate in saliva which overcome swallowing problem especially for pediatric patients. So, even elder people who have swallowing or chewing difficulties experience ease of administration. Moreover these tablets have sufficient mechanical integrity to withstand rigors of mechanical shocks during processing and shipment without breakage.

Materials and methods

Fexofenadine HCl was obtained from Aurobindo Pharmaceuticals, Hyderabad, India., crosscarmellose sodium, crosprovidone, pearlitol SD 200 was a gift from Signet Chemicals., Mumbai., kyron T-314was a gift from Corel Pharmachem., Ahemdabad., microcrystalline cellulose and aerosol was purchase from Modern Scientific, Nasik., aspartame and magnesium stearate was purchase from SD Fine Chemicals, Mumbai, India.

Drug Polymer Compatibility Study

In order to study possible incompatibilities between drug and superdisintegrants, IR spectrums fexofenadine HCl , kyron T-314 and it's physical mixture were recorded in the stretching frequency range 400-4000 cm^{-1}. The samples were prepared by KBr press pellet technique.

Evaluation of Tablet Blend

Tablet blend was evaluated by angle of repose, bulk density, tapped density, Carr's index and Hausner's ratios. Each analysis was carried out in triplicate.

Preparation and compression of tablets

Required quantity of each ingredient was taken for each specified formulation. All the ingredients were passed through mesh 60. The ingredients depicted in Table 1 were mixed homogenously and co grind in a mortar and pestle. Finally, magnesium stearate was added and mixed for 5 min. The mixed blend of drug and excipients was compressed using cadmach single punch tablet punching machine to produce convex faced tablets weighing 150 mg each with a diameter of 8mm.

Evaluation of Tablet

The prepared tablets were evaluated for hardness, thickness, friability, weight variation, wetting time, disintegration time and drug content.

In- vitro drug release studies

The developed formulations (n=3) were subjected to release studies using USP type II dissolution apparatus at 50 rpm with a constant temperature water bath at 37 C±2 C. Dissolution medium used was pH 6.8 (900 ml) for 2, 4, 6, 8, 10, 12, 14, 16, 18, 20 min. Withdraw 10 ml of samples at different time interval and replaced with an equivalent amount of fresh medium. The concentration of fexofenadine HCl was determined by measuring the absorbance at 222 nm.

Wetting time

The wetting time of tablets was measured using a simple procedure. A piece of tissue paper folded twice was placed in a small petri dish containing 10 ml of pH 6.8 buffer solution. A tablet having amaranth powder on the upper surface was placed on the filter paper. Time required to develop red color on the upper surface of tablet was recorded as wetting time.

Result and Discussion

Drug Polymer Compatibility Studies

Fourier Transform Infra-Red Studies

Drug polymer compatibility study was carried out by Fourier Transform Infra-Red Studies. The IR spectrum of pure drug, kyron T-314, and its physical mixture are shown in Figure No.1-3. From the result, it was observed that there is no significant changes in material characteristics when fexofenadine HCl was used with kyron T-314.

Characterization of Tablet Blend

The formulations F1 to F9 were evaluated for angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio. The results are shown in Table No.2. From the Table No.2, the angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio were found to be within the limits. The compressibility index was the lowest for all the formulations which had good flow properties. Also, lower values for Hausner ratio indicate excellent flow properties of the formulations.

Characterization of Formulation

The hardness, thickness, friability, weight variation and drug content of all the formulations were determined and the results obtained are mentioned in the Table No.3-5. The tablets evaluated for the weight variation showed within the limit. The friability of the tablets was found to be less than 1% which was

considered within the limit. The drug content of the formulations was found to be within the limits.

In-vitro Drug Release Studies

Effect of Crosscarmellose

In order to investigate the effect of crosscarmellose on fexofenadine HCl, the formulation F1-F3 were prepared with crosscarmellose in the concentration range of 2, 3, 4 % w/w. The results of release profile are shown in Figure No.4. From the Figure No.4, it was observed that the formulation F1, F2 and F3 showed drug release rate 93.12%, 94.09%, 94.84% in 20 min. From the results, it was observed that the disintegration time of tablet decreases as the concentration of the superdisintegrants increases. Other workers also reported the same result [10-11].

Effect of Crosspovidone

In order to investigate the effect of crosspovidone on fexofenadine HCl, the formulation F4-F6 were prepared with crosspovidone in the concentration range of 2, 3, 4 % w/w. The results of release profile are shown in Figure No. 5. From the Figure No.5, it was observed that formulation F4, F5 and F6 showed drug release rate 94.15%, 95.29%, 96.26% in 20 min. This is because, as the concentration of superdisintegrants increases as the disintegration time decreases [12].The formulation prepared with crosspovidone showed more drug release as compared to the crosscarmellose. The reason behind this, crosscarmellose is generally used as a superdisintegrants but crosspovidone is used as a superdisintegrants as well as solubility enhancing agent [13].Because of this the formulation F4-F6 showed more drug release rate as and disintegrate fastly as compare to formulation prepared by crosscarmellose. Thus crosspovidone shows more release as compare to crosscarmellose.

Effect of Kyron T-314

In order to investigate the effect of kyron T 314 on fexofenadine HCl, the formulation F7-F9 were prepared with Kyron T-314 in the concentration range of 1, 2, 3% w/w. the result of release profile are shown in Figure No. 6.

From the Figure No. 6, it was observed that formulation F7, F8, F9 shows drug release rate 95.58%, 96.32% and 97.46% in 20 min. this indicates that as concentration of superdisintegrant increases the disintegration time decreases. The formulation prepared with kyron T-314 showed more drug release as compared to crosspovidone. This result might be because of it having high swelling index as compared to crosspovidone.[14]

Conclusion

From the study it is concluded that, fast dissolving tablet of fexofenadine HCl can be successfully prepared by direct compression techniques using selected superdisintegrants for better patient compliance and effective therapy. The formulation F9 which is prepared with kyron T-314 in the concentration of 3% is considered as a optimized batch. Disintegration studies indicated that disintegration time were decreased by increasing the concentration of superdisintegrants in following manner.

Kyron T-314 < Crosspovidone < Crosscarmellose

Fast dissolving tablet of fexofenadine HCl of acceptable texture and sufficient structural integrity is successfully prepared by the cost effective direct compression technology.

List of abbreviations

NDDS- Novel Drug Delivery Systems
FDT- Fast Dissolving Tablet
HCl - Hydrochloric acid
FTIR- Fourier transform infrared spectroscopy

Author's contributions

Mr. K. Y. Desale - Carried out experimental part of study.
Ms. P.D. Gaikwad and Dr.V.H. Bankar - Substantial contribution to conception and design, or acquisition of data, or analysis and interpretation of data, also involved in drafting or revising it critically for important intellectual content and given final approval of the version to be published.

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Table No.1 Formulation Composition

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Fexofenadine HCl	30	30	30	30	30	30	30	30	30
Microcrystalline Cellulose	38	36.5	35	38	36.5	35	39.5	38	36.5
Crosscarmellose	3	4.5	6	-	-	-	-	-	-
Crosprovidone	-	-	-	3	4.5	6	-	-	-
Kyron T-314	-	-	-	-	-	-	1.5	3	4.5
Pearlitol SD 200	68	68	68	68	68	68	68	68	68
Aspartame	7	7	7	7	7	7	7	7	7
Aerosil	2	2	2	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2	2	2	2

Table No. 2. Results of Tablet Blend

Formulations	Angle of Repose	Bulk Density (gms/cm^3)	Tapped Density (gms/cm^3)	Carr's Index (%)	Hausner's Ratio
F1	38.04 ±0.21	0.766 ±0.03	0.894 ±0.04	14.31	1.16
F2	35.53 ±0.39	0.777 ±0.01	0.905 ±0.03	14.21	1.16
F3	36.02 ±0.33	0.719 ±0.04	0.888 ±0.02	19.05	1.23
F4	33.69 ±0.24	0.733 ±0.02	0.855 ±0.01	14.33	1.16
F5	36.86 ±0.29	0.695 ±0.05	0.850 ±0.03	18.23	1.22
F6	34.82 ±0.47	0.714 ±0.02	0.882 ±0.05	18.98	1.23
F7	32.47 ±0.18	0.690 ±0.01	0.844 ±0.04	18.29	1.22
F8	34.28 ±0.25	0.755 ±0.02	0.888 ±0.02	15.00	1.17
F9	31.75 ±0.19	0.733 ±0.04	0.855 ±0.01	14.26	1.16

Table No 3. Results of Characterization of Formulations F1-F3

Evaluation Parameter	F1	F2	F3
Weight Variation (mg)	149.33±0.37	149.10±0.17	150.11±0.09
Thickness (mm)	2.21±0.4	2.23±0.06	2.20±0.15
Hardness (kg/cm^2)	4.2±0.2	3.9±0.3	3.4±0.4
% Friability	0.52±0.01	0.69±0.03	0.49±0.02
Content Uniformity (%)	99.21±0.5	99.0±0.2	99.14±0.3
Wetting time (sec.)	42.67±0.35	33.57±0.77	26.30±0.63
Disintegration time (sec.)	46.33±0.57	37.53±1.04	29.00±1.15

Mean ± SD, n=3

Table No 4. Results of Characterization of Formulations F4-F6

Evaluation Parameter	F4	F5	F6
Weight Variation (mg)	151.00±0.96	149.93±0.12	148.22±0.96
Thickness (mm)	2.23±0.05	2.20±0.27	2.22±0.29
Hardness (kg/cm^2)	3.8±0.5	3.5±0.4	3.4±0.2
% Friability	0.56±0.04	0.77±0.05	0.590±0.02
Content Uniformity (%)	99.13±0.4	99.42±0.4	99.01±0.3
Wetting time (sec.)	42.27±1.23	29.31±1.64	24.14±0.77
Disintegration time (sec.)	46.67±0.48	32.28±1.08	28.00±1.20

Mean ± SD, n=3

Table No 5. Results of Characterization of Formulations F7-F9

Evaluation Parameter	F7	F8	F9
Weight Variation (mg)	151.11±0.22	150.20±0.04	151.12±0.09
Thickness (mm)	2.21±0.54	2.24±0.33	2.22±0.28
Hardness (kg/cm^2)	4.1±0.3	3.9±0.5	3.7±0.3
% Friability	0.66±0.01	0.64±0.04	0.71±0.05
Content Uniformity (%)	99.21±0.2	99.13±0.4	99.19±0.5
Wetting time (sec.)	36.40±0.93	33.60±1.22	19.20±0.72
Disintegration time (sec.)	40.20±0.57	37.58±1.45	23.33±0.55

Mean ± SD, n=3

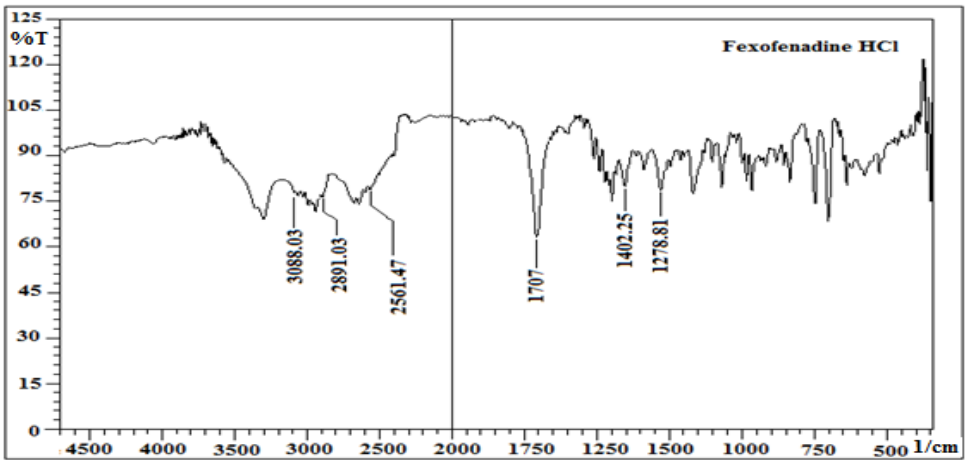

Figure No 1. FTIR Spectra of Fexofenadine HCl

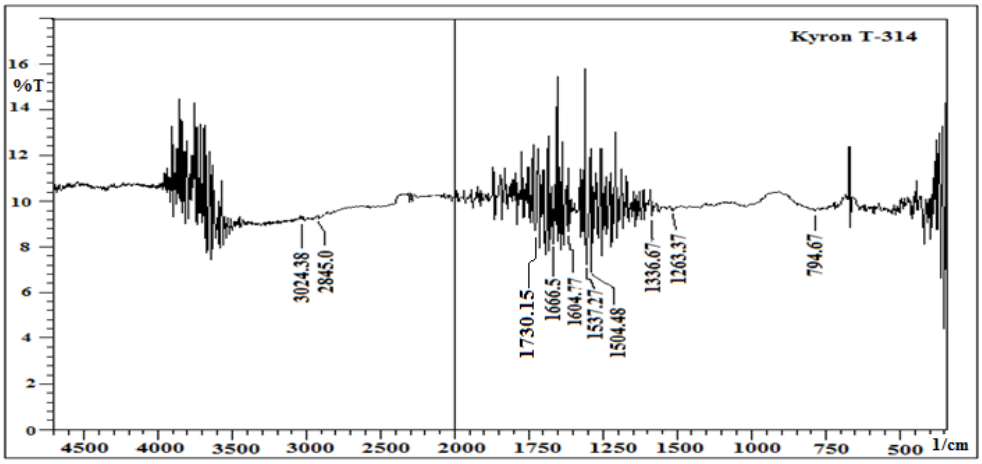

Figure No 2. FTIR Spectra of Kyron T-314

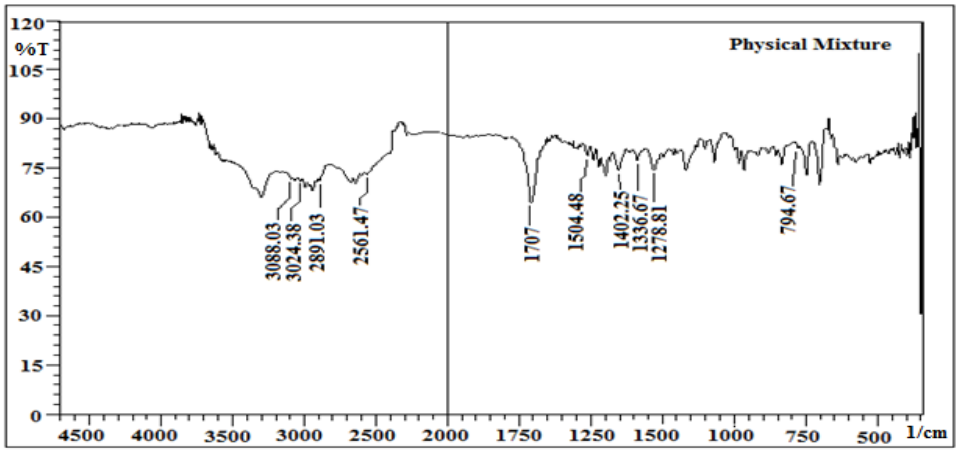

Figure No 3. FTIR Spectra of Physical Mixture

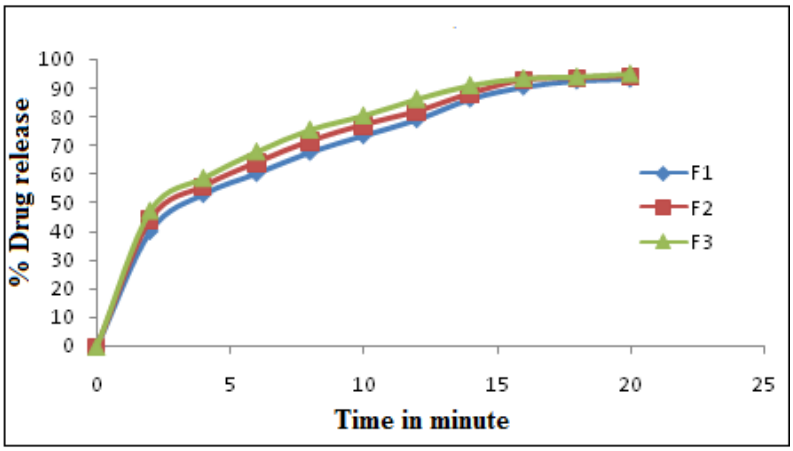

Figure No 4. Results of *in-vitro* Drug Release Profile of F1- F3

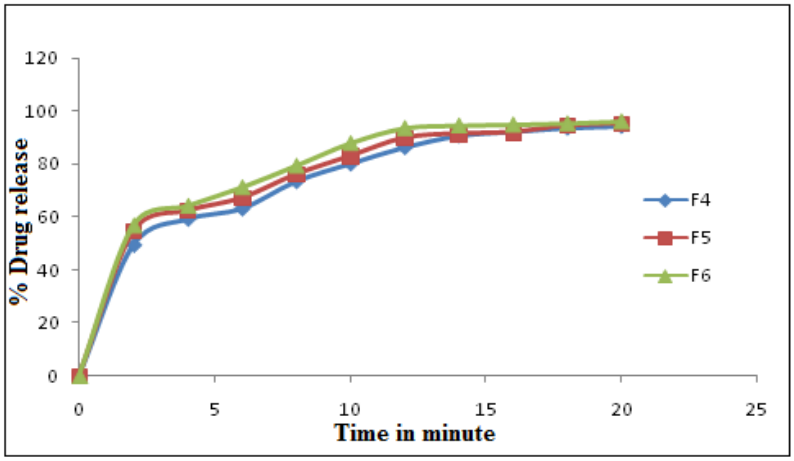

Figure No 5. Results of *in-vitro* Drug Release Profile of F4- F6

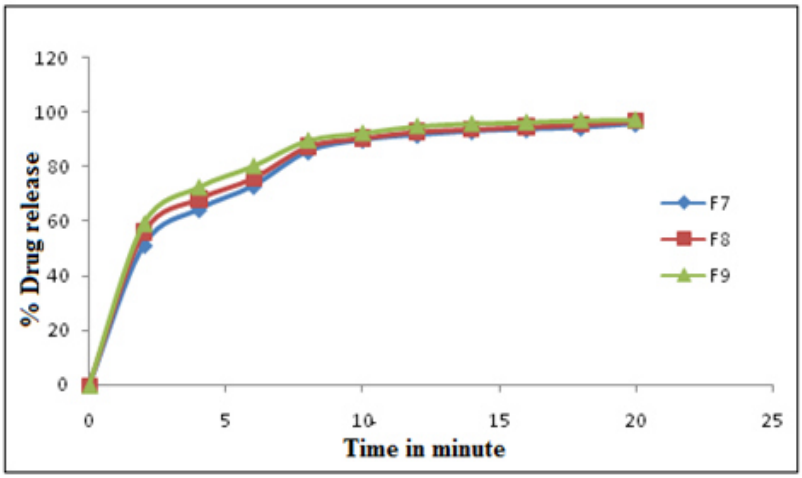

Figure No 6. Results of *in-vitro* Drug Release Profile of F7- F9