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Formulation and evaluation of fexofenadine oral disintegration tablets for improvising patient compliance

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ABSTRACT

One important drawback of solid dosage forms is the difficulty in swallowing or chewing in some patients particularly pediatric and geriatric patients. Hence, the main aim of this study is to formulate Oral Disintegrating Tablets of Fexofenadine to achieve rapid dissolution, absorption and further improving the bioavailability of the drug. Dissolution test was carried out using USP rotating paddle method (apparatus 2). The stirring rate was 50 rpm. 6.8 pH phosphate buffer was used as dissolution medium (900ml) and was maintained at 37 ± 1^0C. Samples of 5ml were withdrawn at pre – determined intervals (2, 4, 6, 8, 10, 15, 20, 25, 30 min), filtered and replaced with 5ml of fresh dissolution medium. The collected samples were suitably dilutedwith dissolution fluid, where ever necessary and were analyzed for the Fexofenadine at 412 nm by using UV spectrophotometer. Oral disintegrating Tablets and Films of Fexofenadine were designed with a view to enhance the patient compliance and provide a quick onset of action. Hence it is very conducive to prepare the oral disintegration tablets of fexofinidine.

Keywords: Oral disintegration tablets, Fexofinidine, Improvising patient's compliance.

INTRODUCTION

Oral administration is the most well known route of administration, around 50-60% of aggregate dosage forms are directed because of simplicity of ingestion, torment evasion, flexibility, and in particular patient consistence. Solid oral delivery systems don't require sterile conditions and are in this manner more affordable to manufacture1.One critical disadvantage of solid dosage forms is the trouble in swallowing (dysphasia) or biting in a few patients especially pediatric and geriatric patients[1-10]. The issue of swallowing is basic marvel in geriatric patient because of fear of choking, hand tremors, dysphasia and in youngsters' because of immature solid and sensory systems and in schizophrenic patients bringing about poor consistence with oral tablet drug therapy which prompts lessened general

therapy adequacy. Troubles in swallowing of tablet and container additionally happen when water isn't accessible, in looseness of the bowels, hacking amid the normal unfavorably susceptible condition and bronchial disease.

Oral fast dissolving drug delivery system (OFDDS) is one such novel way to deal with increment buyer acknowledgment by goodness of quick deterioration, self-administration without water or chewing.Orally disintegrating tablets (ODT) are solid unit dosage forms like traditional tablets, yet are made out of superdisintegrants, which help them to crumble the tablet quickly in salivation without the need to take it water. Orally disintegrating tablets (ODT) are not just shown for individuals who have swallowing challenges, yet additionally are perfect for dynamic individuals.

United States Food and drug administration (FDA) characterized ODT as "a solid dosage shape containing therapeutic substance or dynamic fixing which crumbles quickly as a rule inside a matter of seconds when set upon the tongue [11-15]."

MATERIALS AND EQUIPMENTS

The fexofinadine and other ingredients are obtained as gift sample form the Hetero drugs Ltd, Hyderabad

Preparation of Standard Graph

A standard graph of pure drug in suitable medium was prepared by plotting the concentrations on X – axis and absorbance on Y – axis.

Table 1: Calibration curve for the estimation of Fexofenadine

S.NO.	Concentration(µg/ml)	UV Absorbance (n=5)
1	5	0.132
2	10	0.242
3	15	0.395
4	20	0.528
5	25	0.656
6	30	0.813

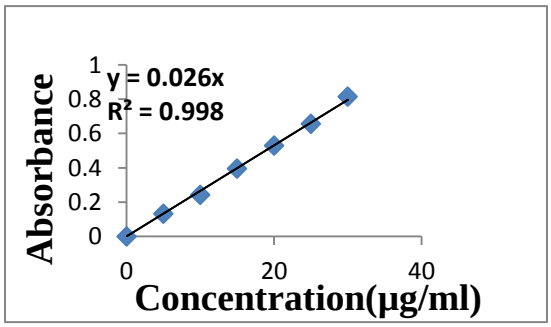

Figure 1: Calibration curve for the estimation of Fexofenadine

The present analytical method obeyed Beer's law in the concentration range of 5 – 30 µg/ml and is suitable for the estimation of Fexofenadine form different solutions. The correlation coefficient (r) value for the linear regression equation was found to be 0.998, indicating a positive correlation between the concentration of Fexofenadine and its corresponding absorbance values [16-19].

Formulation and evaluation of Oral Disintegrating Tablets of Fexofenadine

Fexofenadine ODTs were prepared using direct compression technique. Direct compression technique is a convenient method but the excipients used in this method are costlier when compared to the excipients used in the wet granulation technique. Super disintegrant is varied with 4 different concentrations, (i.e., 3, 6, 9, 12% respectively) keeping all other ingredients constant, there are assigned with formulation codes shown in Table.

Table 2: Formulation codes of ODT

Disintegrant used	Concentration (%)	Formulation code
Crosspovidone	3	F1
	6	F2
	9	F3
	12	F4
Croscarmellose sodium	3	F5
	6	F6
	9	F7
	12	F8
Sodium starch glycolate	3	F9
	6	F10
	9	F11
	12	F12
Crosspovidone + crosscarmellose sodium	6 (3:3)	F13
	8 (4:4)	F14
	10 (5:5)	F15
	12 (6:6)	F16
Crosspovidone + sodium starch glycolate	6 (3:3)	F17
	8 (4:4)	F18
	10 (5:5)	F19
	12 (6:6)	F20

All the required ingredients were passed through 40 mesh to get uniform size particles and weighed accurately. Whole amount of drug, pearlitol SD 200, Avicel pH 102, sodium saccharine and flavour except lubricant were mixed in the increasing order of their weights in a mortar. To this mixture talc and sodium stearyl fumarate were added. The final mixture was shaken manually for 5-10 minutes in a plastic bag. This powder was passed through the hopper of 16 station rotary tabletting machine and punched into tablets using 5 mm s/c. The process is similar for all the formulations, which are prepared by direct compression technique.

Evaluation of orally disintegration tablet formulations

Different quality control tests were performed for all the ODT formulations to check whether these have met the specifications given in USP along with other In *vitro* tests like wetting time and water absorption ratio.

Various *In vitro* tests performed are

- Weight variation test
- Thickness measurement
- Hardness and Friability
- Assay
- Wetting time and Water absorption ratio
- Disintegration Time
- Dissolution test

Dissolution test

Dissolution test was carried out using USP rotating paddle method (apparatus 2). The stirring rate was 50 rpm. 6.8 pH phosphate buffer was used as dissolution medium (900ml) and was maintained at 37 ± 1^0C. Samples of 5ml were withdrawn at pre – determined intervals (2, 4, 6, 8, 10, 15, 20, 25, 30 min), filtered and replaced with 5ml of fresh dissolution medium. The collected samples were suitably diluted with dissolution fluid, where ever necessary and were analyzed for the Fexofenadine at 412 nm by using UV spectrophotometer [20-27]. Each dissolution study was performed for three times and mean values were taken.

Table 3: Formulae of Fexofenadine ODTs prepared by direct compression method with various superdisintegrants

Ingredients	Super disintegrants concentration (%) of Crosspovidone/ Croscarmellose Sodium/ Sodium Starch Glycolate			
	3%	6%	9%	12%
Fexofenadine	30	30	30	30
Superdisintegrants	3	6	9	12
Avicel PH 102	44	41	38	35
Pearlitol SD200	10	10	10	10
Sodium saccharin	10	10	10	10
Orange flavor	2	2	2	2
Sodium stearyl fumerate	0.5	0.5	0.5	0.5
Talc	0.5	0.5	0.5	0.5
Total weight (mg)	100	100	100	100

Table 4: Preformulation characteristics of Fexofenadine ODTs

Formulation	Bulk density (g/cc)	Tapped density (g/cc)	Hausner ratio	Compressibilty index (%)	Angle of repose (ɵ)
F1	0.435	0.522	1.20	16.66	32.67
F2	0.429	0.518	1.20	17.18	29.08
F3	0.430	0.524	1.21	17.93	31.78
F4	0.432	0.528	1.22	18.18	30.64
F5	0.428	0.518	1.21	17.37	30.36
F6	0.420	0.510	1.21	17.64	31.05
F7	0.416	0.509	1.22	18.27	32.54
F8	0.417	0.515	1.23	19.02	29.67
F9	0.425	0.515	1.21	17.47	31.85
F10	0.421	0.509	1.20	17.28	29.56
F11	0.419	0.515	1.22	18.64	30.17
F12	0.415	0.512	1.23	18.94	32.08

Table 5: Tabletting characteristics of Fexofenadine ODTs

Formulation	Weight (mg)	Drug content (%)	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)
F1	99.9±0.70	98.96±0.47	3.05±0.13	0.48	2.84±0.032
F2	99.52±0.85	99±0.65	3.10±0.15	0.53	2.85±0.028
F3	98.9±0.52	99.11±0.52	2.95±0.08	0.44	2.86±0.024
F4	100.2±1.17	99.15±0.60	2.95±0.10	0.57	2.86±0.051
F5	99.0±0.49	99.2±0.4	3.08±0.12	0.43	2.88±0.048
F6	98.8±0.58	98.85±0.58	3.11±0.14	0.56	2.90±0.052
F7	99.3±0.54	99.31±0.24	2.92±0.08	0.53	2.92±0.038
F8	100.4±1.0	98.96±0.28	3.0±0.09	0.45	2.91±0.042
F9	99.6±0.95	99.3±0.38	2.9±0.07	0.6	2.90±0.040
F10	99.2±0.97	99.36±0.29	3.05±0.08	0.49	2.89±0.042
F11	99.4±0.86	98.75±0.40	3.05±0.09	0.53	2.89±0.034
F12	98.5±0.42	99.21±0.38	2.93±0.08	0.58	2.87±0.031

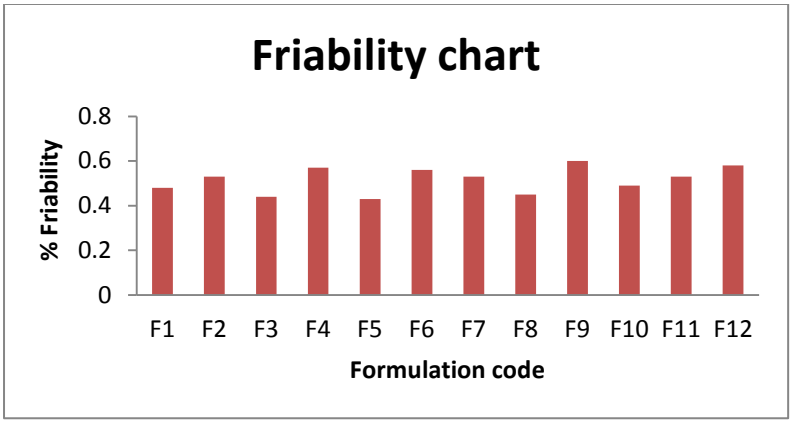

Figure 2: Graphical representation of friability of Fexofenadine ODTs prepared by varying concentrations of superdisintegrants

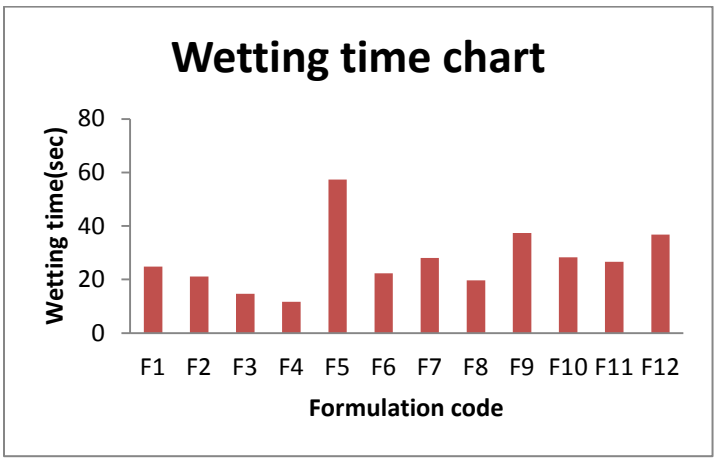

Figure 3: Graphical representation of wetting time of Fexofenadine ODTs prepared by varying concentrations of superdisintegrants

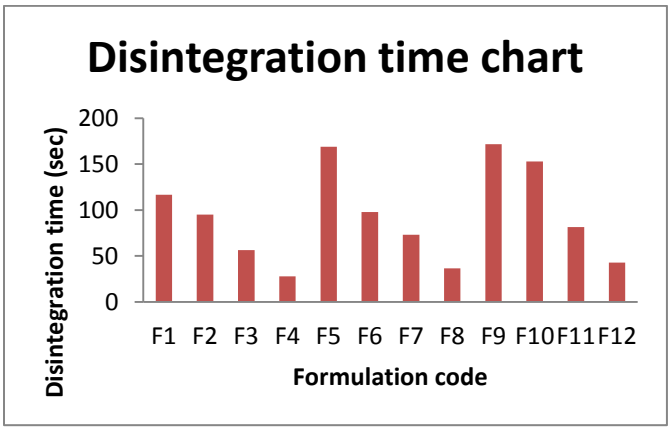

Figure 4: Graphical representation of disintegration times of Fexofenadine ODTs prepared by varying concentrations of superdisintegrants

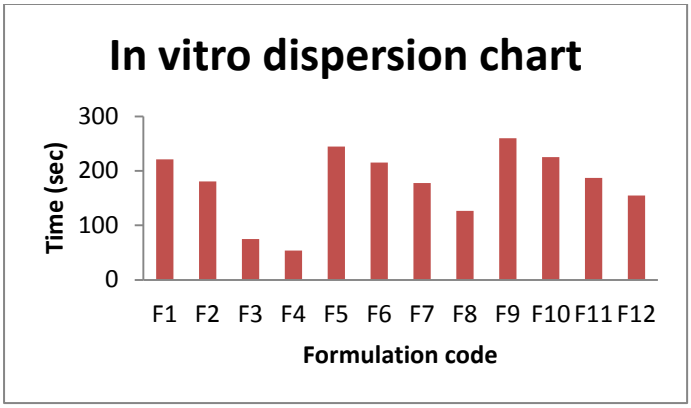

Figure 5: Graphical representation in vitro dispersion times of Fexofenadine ODTs prepared by varying concentrations of superdisintegrants

Table 6: Cumulative percent Fexofenadine released from ODTs containing varying concentrations of different superdisintegrants (F1-F6)

Cumulative percent (±S.D.) drug released						
Time (min)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
2	27.35±0.28	22.35±0.52	20.46±0.25	28.31±0.23	18.35±0.34	15.43±0.30
4	40.33±0.28	34.36±0.28	29.28±0.19	41.33±0.24	25.5±0.28	23.43±0.32
6	55.46±0.31	45.31±0.27	42.35±0.25	59.33±0.26	37.36±0.25	37.36±0.26
8	69.46±0.27	62.35±0.25	61.31±0.23	73.48±0.34	57.41±0.23	54.38±0.26
10	74.38±0.27	75.48±0.30	76.4±0.36	85.38±0.34	64.55±0.28	67.38±0.37
15	83.35±0.20	87.4±0.31	82.53±0.30	98.6±0.29	72.48±0.35	75.46±0.26
20	94.45±0.30	96.31±0.29	97.31±0.20	98.89±0.32	80.45±0.28	82.31±0.23
25	94.89±0.24	96.57±0.28	97.76±0.28	98.95±0.24	86.5±0.26	87.48±0.24
30	95.78±0.27	96.85±0.32	97.96±0.25	98.99±0.23	89.53±0.19	92.36±0.25

Table 7: Cumulative percent Fexofenadine released from ODTs containing varying concentrations of different superdisintegrants (F7-F12)

Cumulative percent (±S.D.) drug released						
Time (min)	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
2	22.33±0.25	14.38±0.31	19.33±0.20	23.43±0.16	18.48±0.33	19.4±0.32
4	33.36±0.31	22.1±0.59	28.36±0.32	35.31±0.27	27.18±0.18	27.41±0.26
6	45.46±0.26	36.43±0.30	36.45±0.25	47.36±0.29	34.43±0.23	35.28±0.29
8	62.43±0.23	55.46±0.30	49.43±0.26	53.5±0.34	45.61±0.17	52.43±0.26
10	70.28±0.20	62.46±0.25	55.48±0.26	64.45±0.30	52.41±0.36	65.41±0.33
15	78.41±0.26	75.58±0.27	68.46±0.32	72.6±0.27	61.25±0.55	78.45±0.35
20	86.28±0.24	80.4±0.26	74.58±0.27	78.41±0.14	70.46±0.21	84.51±0.24
25	90.28±0.17	83.48±0.30	78.43±0.27	83.45±0.28	75.41±0.24	88.36±0.18
30	94.46±0.25	95.43±0.19	85.4±0.22	88.45±0.18	90.4±0.33	92.38±0.19

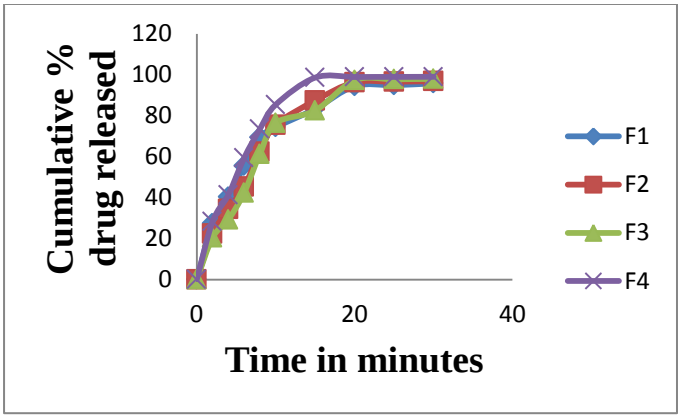

Figure 6: Graphical representation of Cumulative percent Fexofenadine released from ODTs containing varying concentrations of crosspovidone.

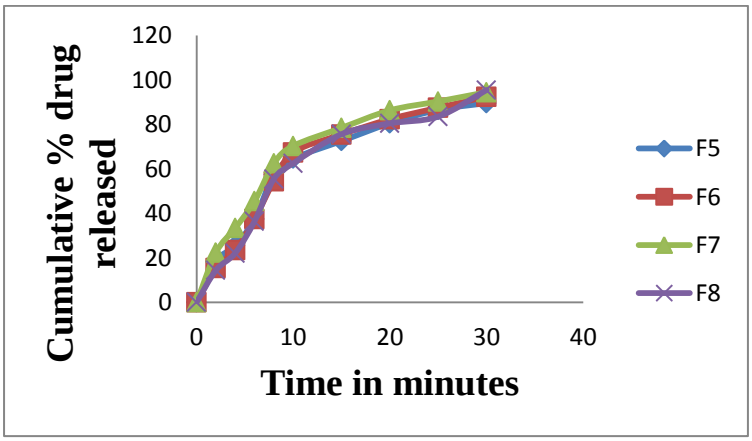

Figure 7: Graphical representation of Cumulative percent Fexofenadine released from ODTs containing varying concentrations of croscarmellose sodium.

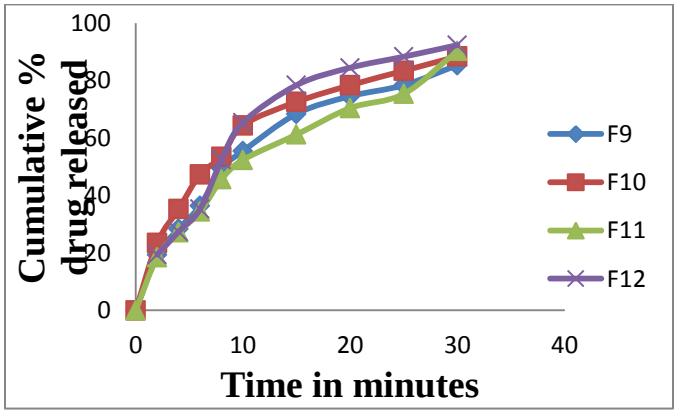

Figure 8: Graphical representation of Cumulative percent Fexofenadine released from ODTs containing varying concentrations of sodium starch glycolate.

Table 8: Formulae of Fexofenadine ODTs prepared with combination of superdisintegrants

Ingredients	CP + CCS				CP + SSG			
	6%	8%	10%	12%	6%	8%	10%	12%
Fexofenadine	30	30	30	30	30	30	30	30
Superdisintegrants	6	8	10	12	36	48	60	72
Avicel PH 102	41	39	37	35	41	39	37	35
Pearlitol SD200	10	10	10	10	10	10	10	10
Sodium saccharine	10	10	10	10	10	10	10	10
Orange flavor	2	2	2	2	2	2	2	2
Sodiumstearyl fumerate	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Talc	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Total weight (mg)	100	100	100	100	100	100	100	100

Note: CP – Crosspovidone, CCS – Croscarmellose Sodium, SSG – Sodium Starch Glycolate

Table 9: Preformulation characteristics of Fexofenadine ODTs prepared with combination of superdisintegrants

Formulation	Bulk density (g/cc)	Tapped density (g/cc)	Hausner ratio	Compressibilty index (%)	Angle of repose (ɵ)
F13	0.420	0.520	1.23	19.23	29.67
F14	0.423	0.512	1.21	17.38	29.54
F15	0.435	0.520	1.20	16.34	31.76
F16	0.422	0.512	1.21	17.57	32.04
F17	0.425	0.523	1.23	18.73	30.56
F18	0.434	0.526	1.21	17.49	31.23
F19	0.426	0.512	1.20	16.79	29.52
F20	0.420	0.519	1.23	19.07	29.32

Table 10 Tabletting characteristics of Fexofenadine ODTs prepared with combination of superdisintegrants

Formulation	Weight (mg)	Drug content (%)	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)
F13	100.3±1.18	98.56±0.49	3.19±0.05	0.47	2.86±0.034
F14	99.3±0.53	98.61±0.60	3.16±0.04	0.52	2.86±0.023
F15	100.1±0.75	98.98±0.56	3.10±0.10	0.63	2.87±0.044
F16	100.3±0.86	99.03±0.58	3.05±0.09	0.58	2.89±0.051
F17	99.1±0.84	97.75±0.69	3.15±0.04	0.58	2.85±0.029
F18	98.8±0.56	98.76±0.56	2.92±0.08	0.53	2.88±0.046
F19	99.6±0.60	99.08±0.29	3.00±0.09	0.51	2.86±0.025
F20	100.0±0.75	98.86±0.39	3.12±0.12	0.55	2.84±0.034

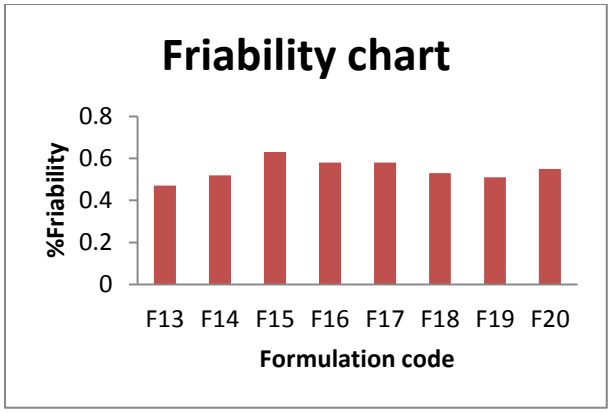

Figure 9: Graphical representation of friability of Fexofenadine ODTs prepared by varying concentrations of combination of superdisintegrants

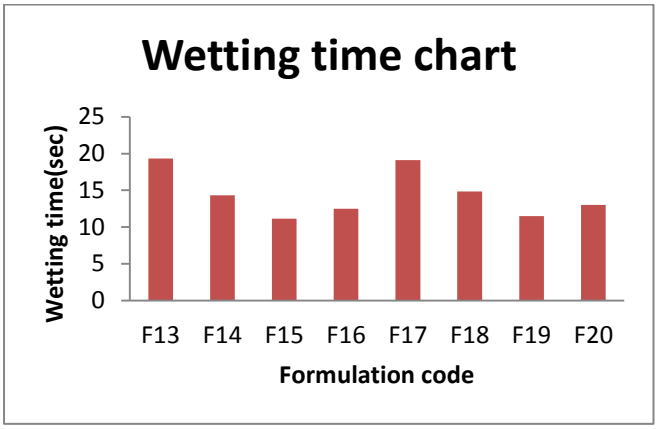

Figure 10: Graphical representation of witting time of Fexofenadine ODTs prepared by varying concentrations of combination of superdisintegrants

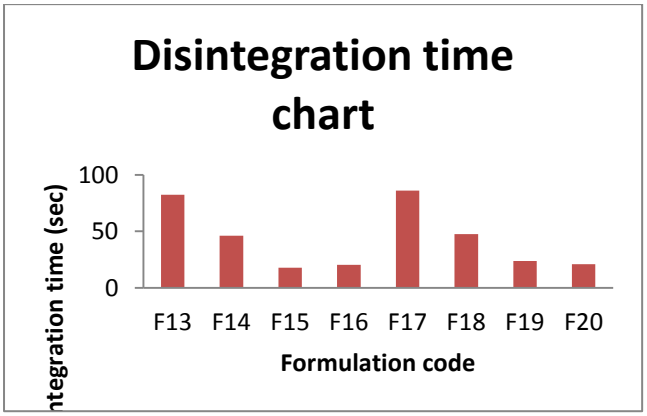

Figure 11: Graphical representation of disintegration times of Fexofenadine ODTs prepared by varying concentrations of combination of superdisintegrants

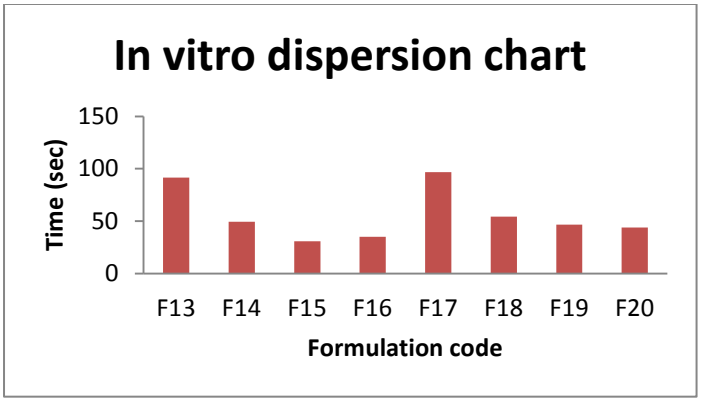

Figure 12: Graphical representation of *in vitro* dispersion times of Fexofenadine ODTs prepared by varying concentrations of combination of superdisintegrants

Table 11: Cumulative percent Fexofenadine released from ODTs prepared by varying concentrations of combination of superdisintegrants (F13-F16)

Cumulative percent (±S.D.) drug released				
Time (min)	**F13**	**F14**	**F15**	**F16**
2	17.41±0.26	26.21±0.17	25.43±0.29	21.4±0.24
4	25.43±0.25	32.38±0.21	37.41±0.31	31.43±0.33
6	37.43±0.33	45.31±0.27	51.36±0.28	40.25±0.18
8	53.45±0.26	60.25±0.15	68.35±0.31	64.45±0.28
10	66.43±0.24	75.31±0.29	77.35±0.28	71.53±0.26
15	78.45±0.24	87.48±0.24	89.4±0.2	79.46±0.22
20	83.45±0.24	89.31±0.17	93.38±0.24	84.53±0.25
25	85.35±0.25	96.52±0.19	99.87±0.18	89.55±0.16
30	94.5±0.21	------	------	96.38±0.24

Table 12: Cumulative percent Fexofenadine released from ODTs prepared by varying concentrations of combination of superdisintegrants (F17-F20)

Cumulative percent (±S.D.) drug released				
Time (min)	**F17**	**F18**	**F19**	**F20**
2	13.48±0.27	24.55±0.32	24.35±0.30	26.3±0.28
4	25.35±0.30	35.3±0.28	31.41±0.25	38.3±0.28
6	33.4±0.20	42.4±0.31	43.53±0.21	50.36±0.24
8	50.38±0.18	53.38±0.27	57.43±0.33	61.48±0.21
10	61.4±0.30	65.43±0.35	69.53±0.24	69.35±0.28
15	75.55±0.32	76.5±0.28	77.48±0.34	76.51±0.17
20	77.43±0.29	82.45±0.30	85.38±0.23	81.48±0.24
25	82.45±0.18	86.5±0.26	91.45±0.18	84.45±0.27
30	88.56±0.21	92.5±0.14	95.48±0.18	94.51±0.19

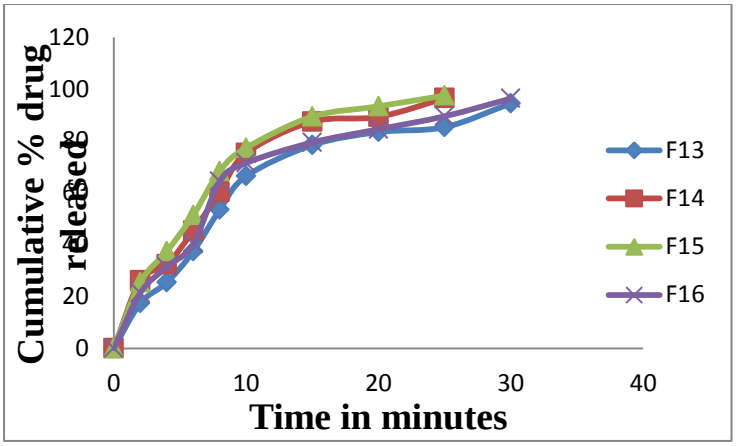

Figure 13: Graphical representation of Cumulative percent Fexofenadine released from ODTs containing varying concentrations of CP + CCS

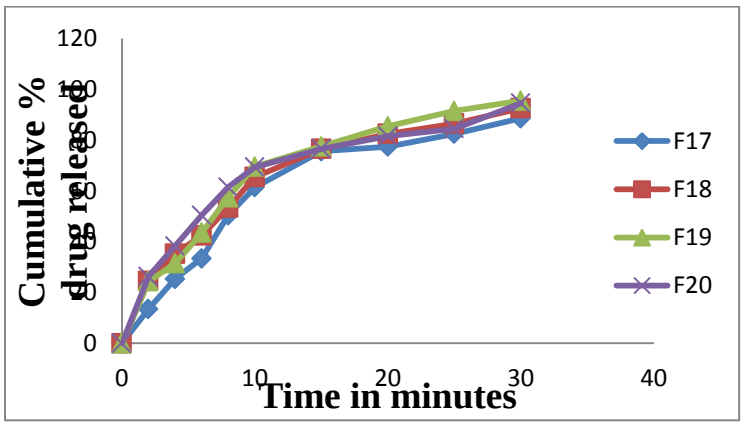

Figure 14: Graphical representation of Cumulative percent lisinopril released from ODTs containing varying concentrations of CP + SSG

Disintegration time is considered to be important criteria in selecting the best ODT formulation. The *in vitro* disintegration time for all the twenty formulations varied from 17.66±0.51 to 171.83±1.16 seconds. The rapid disintegration was seen in the formulations containing crosspovidone and formulations containing combination of superdisintegrants (CP + CCS, CP + SSG). This is due to rapid uptake of the water from the medium, swelling and burst effect. It is also noticed that as the disintegrant concentration was increased from 9 to 12% the time taken for disintegration was reduced. The disintegration time of formulation (F15) containing 5% CP + 5% CCS was found to be lower (17.66±0.51) and was selected as the best ODT formulation among all the 20 formulations.

In vitro dispersion is a special parameter in which the time taken by the tablet for complete dispersion is measured. The time for all the twenty formulations varied between 30.66±0.81 and 259.83±1.47 sec.

The development of dissolution method for ODTs is almost similar to the approach taken for conventional tablets until they utilize the taste masking. The taste masking aspect greatly influences dissolution method development, specifications, and testing. Several factors like varied thickness and pH dependent solubility of drug particle coating influence dissolution profiles of ODTs containing taste masked actives. Since Fexofenadine is not bitter in taste, the metallic taste of drug was masked by using sweeteners and flavors. It has been reported that USP type II apparatus with a paddle speed of 50 rpm is commonly used for ODT formulations. Slower

paddle speeds are utilized to obtain good profiles as these formulations disintegrate rapidly.

In *vitro* dissolution studies of the prepared ODTs was performed in pH 6.8 phosphate buffer using USP dissolution apparatus type 2. The dissolution rate was found to increase linearly with increasing concentration of superdisintegrant. Formulations F1, F2, F3 and F4 which contained increasing concentrations of crosspovidone have recorded drug release 95.78%, 96.85%, 97.96 and 98.99% respectively within 20 to 30 min. Formulations F5, F6, F7 and F8 which contained increasing concentrations of croscarmellose sodium have recorded drug release 89.53%, 92.36%, 94.46% and 95.43% respectively, at the end of 30 min. Formulations F9, F10, F11 and F12 which contained increasing concentrations of sodium starch glycolate have recorded drug release 85.4%, 88.45%, 90.4% and 92.38% respectively, at the end of 30 min.

Formulations F13, F14, 15 and F16 which contained increasing concentrations of combination of CP + CCS have recorded drug release 94.5%, 96.52%, 99.87% and 96.38% respectively, at the end of 25 to 30 min. Formulations F17, F18, F19 and F20 which contained increasing concentrations of combination of CP + SSG have recorded drug release 88.56%, 92.5%, 95.48% and 94.51respectivel, at the end of 30 min.

CONCLUSION

In this current research, Oral Disintegrating Tablets of Fexofenadine were formulated with an aim to improve the versatility, patient compliance and accurate dosing. The formulations ere developed with an objective to use by the pediatric and geriatric patients. Fexofenadine Oral Disintegrating Tablets were prepared by direct compression method using crosspovidone, croscarmellose sodium, sodium starch glycolate superdisintegrants exhibited good preformulation and tabletting properties. Based on disintegration and dissolution results it was concluded that the formulation F15 has best formulation among the all other formulations. The metallic taste of the drug was masked by Sodium saccharin, and Orange flavor which may considerably enhance the patient compliance.

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