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Original Article

FORMULATION AND *IN-VITRO* EVALUATION OF DEFERASIROX ORO-DISPERSIBLE TABLETS

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ABSTRACT

Objective: Deferasirox is a once daily, oral iron chelator approved for treatment of transfusional iron overload in adult and paediatric patients. In case of iron overdose or poisoning, immediate attention deferasirox is required in the systemic circulation to counter act the iron. Hence we feel that formulation of Oro-dispersible tablets of deferasirox is an ideal approach.

Methods: FTIR showed that there is no interaction between drug and excipients. Mouth dissolving tablets of Deferasirox were prepared using crospovidone, croscarmellose and sodium starch glycolate as superdisintegrants by direct compression method. Dissolution of prepared Oro-dispersible tablets of Deferasirox was performed using USP type II apparatus in 6.8 pH phosphate buffer at 50 rpm with temperature being maintained at 37±0.5°C. Samples were withdrawn at 10, 15, 20, 30 and 45min time points and were analysed using UV- visible spectrophotometer at 245 nm.

Results: The tablets prepared were evaluated for various parameters like weight variation, hardness, friability, *in-vitro* dispersion time, drug polymer interaction, drug content, water absorption ratio and wetting time and *in-vitro* release and were found to be within the limits.

Conclusion: Formulation with crospovidone containing superdisintegrants has shown better in-vitro dissolution profile compared with other formulations. In conclusion, development of fast dissolving tablets using superdisintegrants gives rapid drug delivery and rapid onset of action.

Keywords: Oro-dispersible tablets, Superdisintegrants, Deferasirox.

INTRODUCTION

The oral route of administration still continue to be the most preferred route due to its manifold advantages including ease of ingestion, pain avoidance, suppleness and most importantly patient compliance. Most popular dosage form being tablets and capsules, even few of the drawbacks of these dosage forms like swallowing and some drugs resist comparison in dense compacts, owing to their amorphous nature or flocculants, low density characteristics. Drugs with poor wetting, slow dissolution properties, intermediate to large dosage, and optimum absorption in the gastrointestinal tract or any combination of these features may be difficult or impossible to formulate and manufacture as a tablet that will still provide adequate or full drug bioavailability. Bitter tasting drugs, drugs with an objectionable odour, or drugs that are sensitive to oxygen or atmospheric moisture may require encapsulation or entrapment prior to compression. The target population of these dosage forms are paediatric, geriatric, bedridden, developmentally disabled and the patients with tenacious nausea or who have little access to water. Even many patients find it difficult to swallow tablets and hard gelatin capsules and thus do not comply with prescription, which results in high incidence of non-compliance and ineffective therapy.

Recent advances in novel drug delivery systems (NDDS) aim to enhance safety and efficacy of drug molecule by formulation and to achieve better patient compliance. One such approach is 'mouth dissolving tablets' which disintegrate or dissolve in saliva and are swallowed without water as tablet disintegrate in mouth, this could enhance the clinical effect of drug through pre-gastric absorption from the mouth, pharynx, oesophagus, this leads to an increase in the bioavailability by avoiding first pass liver metabolism [1].

These tablets display a fast and spontaneous de-aggregation in the mouth, soon after the contact with saliva, though they can be handled or extracted from the package without alteration. The active agent can thus rapidly dissolve in the saliva and be absorbed through whatever membrane it encounters, during deglutition, unless it is protected from pre-gastric absorption. To fulfill these requirements, tablets must be highly porous, incorporating hydrophilic excipients, able to rapidly absorb water for a rapid deaggregation of the matrix. Different technological techniques, such as freeze drying or molding or direct compression are currently employed to prepare the formulations of this type present on the pharmaceutical market [1,2].

Honda and Nakano reported that a half of the patients surveyed experienced difficulty in taking medication and felt that a tablet was a better and easier formulation compared to other formulations such as capsules or powder. They also reported that the degree of ease when taking a tablet depended on its size. They reported that the size of tablet that was easiest to swallow was 7–8 mm, but the size easiest to handle was one larger than 8 mm [3]. Tanmoy ghosh *et. al.,* exploration on new generation oro-dispersible tablets and its future prospective concluded that future challenges includes reducing costs by finding ways to manufacture with conventional equipment, using versatile packing and improving mechanical strength and taste masking capabilities [4]. Kulkarni maushumi S *et. al.,* formulated and evaluated oro-dispersible tablet of ornidazole, masked microspheres were prepared and then formulated into oro-dispersible tablets using the technique of superdisintegrating addition [5] Shid S. L *et. al.,* formulated effect of superdisintegrants in rapidly disintegrating flurbiprofen sodium oro-dispersible tablets via direct compression and camphor sublimation. Thus it was concluded that the stable oro-dispersible tablets of flubiprofen can be developed for the rapid release of flurbiprofen [6]Khalid K. Abed *et. al.,* formulated Oro-dispersible tablets of diazepam. Diazepam tablets were prepared using different types of superdisintegrants and subliming agents at different concentrations and two methods of preparation by wet granulation and direct compression methods [7] P. V. Swamy *et. al.,* formulated design and evaluation of cost effective oro-dispersible tablets of diethylcarbamazine citrate by effervescent method. In effervescent method mixture of sodium bicarbonate and tartaric acid along with treated agar were used as disintegrants [8] Abdelbary G *et. al.,* formulated and determined the *in-vitro*

disintegration profile of rapidly disintegrating tablets and correlation with oral disintegration. Correlation of *in-vitro* disintegration times is compared with oral times [9].Takao Mizumoto *et. al.,* formulated design of a novel fast-disintegrating tablet having sufficient hardness and manufactured by commonly used equipment.

The process included using of saccharides with high and low compressibility such that to achieve adequate hardness and quick disintegration [10] Indhumathi D. formulated Oro-dissolving tablets by superdisintegrants addition method by using Fluoxetine. The tablets were prepared by wet granulation method and evaluated for hardness, thickness, friability, weight variation uniformity of content, disintegration time and dissolution studies. In-vitro dissolution studies show the release in the following order of superdisintegrants: crospovidone > pregelatinized starch > croscarmellose > sodium starch glycolate [11].

MATERIALS AND METHODS

Preparation of standard graph of Deferasirox in pH 6.8 phosphate buffer

Accurately weighed amount (100 mg) of the drug was dissolved in 5ml of organic solvent like Dimethyl sulfoxide(DMSO), Dimethyl formamide(DMFO) and then dissolved in pH 6.8 phosphate buffer in 100 ml volumetric flask and the volume was made up to 100ml. From this stock solution 10ml is withdrawn in to volumetric flask, made the volume up to 100ml with pH 6.8 buffer.

From this II stock solution (100µg/ml), 20ml is withdrawn and made the volume up to 100ml with distilled water. From this III stock solution different concentration of 2, 4, 6, 8, 10µg/ml solutions were prepared and the corresponding absorbance was measured at 245 nm in a UV/Visible spectrophotometer.

Preparation of Deferasirox Oro-dispersible tablets by Direct compression method

For preparation of deferasirox by direct compression method, the formulation includes different list of excipients which are as follows.

Drug - Deferasirox

Superdisintegrants- Crospovidone, Croscaramellose, Sodium starch glycolate.

Diluents - Lactose, Mannitol, MCC.

Lubricant - Talc

Glidant- Magnesium stearate

Sweetening agents - Sucrose

Flavouring agent- Peppermint oil

The drug, diluent, superdisintegrant, sweeteners, are passed through the sieve no-40#. All the ingredients are mixed well in the motor.

Then mixed with a lubricant for 3 min in a motor and then mixer was compressed by using 10mm flat punches on sixteen station rotary tablet compression machine (Table 1, 2, 3, 4).

RESULTS AND DISCUSSION

Preparation of standard graph of Deferasirox

Deferasirox has the maximum absorbance at 245 nm. Standard graph of Deferasirox in pH 6.8 buffer was plotted by taking concentrations ranging from 2 to 10 µg/ml and a good correlation was obtained with R^2 value of 0.9991.

Table 1: Composition of mouth dissolving tablets of deferasirox (F1-F9) using spray dried lactose as diluent

Formula	F1	F2	F3	F4	F5	F6	F7	F8	F9
Deferasirox(mg)	150	150	150	150	150	150	150	150	150
Crospovidone	2%	4%	6%	-	-	-	-	-	-
Croscarmellose	-	-	-	2%	4%	6%	-	-	-
SSG	-	-	-	-	-	-	2%	4%	6%
Peppermint oil	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%
Colouring agent	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%
Sucrose	2%	2%	2%	2%	2%	2%	2%	2%	2%
Talc	1%	1%	1%	1%	1%	1%	1%	1%	1%
Magnesium stearate	1%	1%	1%	1%	1%	1%	1%	1%	1%
Spray dried lactose	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

Table 2: Composition of mouth dissolving tablet of deferasirox (F10-F18) by using mannitol as diluent

Formula	F10	F11	F12	F13	F14	F15	F16	F17	F18
Deferasirox	150	150	150	150	150	150	150	150	150
Crospovidone	2%	4%	6%	-	-	-	-	-	-
Croscarmellose	-	-	-	2%	4%	6%	-	-	-
SSG	-	-	-	-	-	-	2%	4%	6%
Peppermint oil	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%
Colouring agent	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%
Sucrose	2%	2%	2%	2%	2%	2%	2%	2%	2%
Talc	1%	1%	1%	1%	1%	1%	1%	1%	1%
Magnesium stearate	1%	1%	1%	1%	1%	1%	1%	1%	1%
Mannitol	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

Table 3: Composition of mouth dissolving tablets of deferasirox(F19-F27) by using MCC as diluent.

Formula	F19	F20	F21	F22	F23	F24	F25	F26	F27
Deferasirox	150	150	150	150	150	150	150	150	150
Cross povidone	2%	4%	6%	-	-	-	-	-	-
croscarmellose	-	-	-	2%	4%	6%	-	-	-
SSG	-	-	-	-	-	-	2%	4%	6%
Peppermint oil	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%
Colouring agent	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%
Sucrose	2%	2%	2%	2%	2%	2%	2%	2%	2%
Talc	1%	1%	1%	1%	1%	1%	1%	1%	1%
Magnesium stearate	1%	1%	1%	1%	1%	1%	1%	1%	1%
MCC	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

Table 4: Composition of mouth dissolving tablets of deferasirox (f28-f30) by using combination of superdisintegrants and mannitol as diluents

Formula	F28	F29	F30
Deferasirox(mg)	150	150	150
Crospovidone	5%	-	5%
Croscarmellose	5%	5%	-
SSG	-	5%	5%
Peppermint oil	0.05%	0.05%	0.05%
Colouring agent	0.05%	0.05%	0.05%
Sucrose	2%	2%	2%
Talc	1%	1%	1%
Magnesium stearate	1%	1%	1%
Mannitol	Q.S	Q.S	Q.S

Table 5: Preparation of standard graph of deferasirox in ph 6.8 phosphate buffer

Concentration(µg/ml)	Absorbance
0	0
2	0.3367
4	0.4903
6	0.6669
8	0.8789
10	1.0814
Slope	0.1095
R^2	0.9991

Evaluation of blend

Table 6: Evaluation of mixed blend of drug and excipients

Formula	Angle of repose(θ)	Bulk density (gm/cm³)	Tapped density (gm/cm³)	Compressibility index (I)	Hausner's ratio
F1	28.3±1.7	0.42±0.16	0.66±0.24	39.2	1.5
F2	25.6±1.9	0.38±0.21	0.52±0.16	44.5	0.9
F3	29.4±1.1	0.43±0.13	0.71±0.18	40.2	1.19
F4	26.3±1.3	0.36±0.15	0.62±0.26	36.4	1.2
F5	25.3±1.8	0.41±0.13	0.59±0.24	43.1	0.8
F6	29.4±1.1	0.42±0.12	0.64±0.17	33.3	0.98
F7	30.0±1.2	0.36±0.17	0.59±0.19	35.4	0.7
F8	26.8±1.5	0.4±0.16	0.62±0.14	42.3	1.15
F9	29.3±1.7	0.39±0.23	0.71±0.17	38.1	0.92
F10	30.0±1.3	0.4±0.17	0.58±0.23	40.6	0.97
F11	30.0±1.6	0.37±0.3	0.6±0.16	36.5	0.9
F12	29.7±1.2	0.42±0.15	0.58±0.29	37.2	0.8
F13	27.5±1.2	0.36±0.12	0.59±0.23	40.6	0.91
F14	28.4±1.1	0.42±0.15	0.61±0.16	38.7	1.2
F15	30.2±1.8	0.4±0.14	0.62±0.25	35.4	0.79
F16	30.4±1.4	0.51±0.25	0.71±0.22	39.7	0.83
F17	29.2±1.6	0.39±0.17	0.57±0.13	41.3	0.94
F18	30.0±1.4	0.44±0.15	0.7±0.17	34.9	1.5
F19	28.7±1.4	0.42±0.21	0.62±0.17	40.3	0.9
F20	28.5±1.3	0.39±0.11	0.58±0.12	39.4	0.87
F21	28.4±1.3	0.42±0.13	0.61±0.16	38.7	1.2
F22	30.2±1.3	0.4±0.26	0.62±0.13	35.4	0.79
F23	30.4±1.5	0.51±0.19	0.71±0.19	39.7	0.83
F24	30.0±1.2	0.36±0.16	0.59±0.28	35.4	0.7
F25	26.8±1.7	0.4±0.23	0.62±0.12	42.3	1.15
F26	29.3±1.8	0.39±0.14	0.71±0.22	38.1	0.92
F27	29.2±1.5	0.39±0.18	0.57±0.27	41.3	0.94
F28	29.7±1.5	0.42±0.11	0.58±0.12	37.2	0.8
F29	27.5±1.1	0.36±0.16	0.59±0.23	40.6	0.91
F30	28.5±1.6	0.39±0.13	0.58±0.25	39.4	0.87

Blend was evaluated for bulk density, tapped density, compressibility index, Hausner ratio, angle of repose (Table 6). All the formulations show angle of repose below 30^0 that mean they show free flowing property. All the formulation has Hausner ratios between the 0.7 to1.5. It indicates all the formulations show better flow property.

Table 7: Evaluation of deferasirox tablets

Formulation	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm²)	Friability	Disintegration time(sec)	Water absorption ratio(%)	Drug content(%)
F1	353±1.5	4.62±0.99	3.11±0.03	0.45±0.12	96±5	88.91±0.96	96.4±0.7
F2	351± 1.6	4.55±0.16	3.19±0.22	0.35±0.14	92±5	90.48±0.52	97.3±0.5
F3	351±0.9	4.54±0.35	3.46±0.51	0.37±0.08	94±4	92.58±0.45	94.1±0.6
F4	349±1.8	4.47±0.24	3.27±0.03	0.29±0.19	107±5	91.98±048	98.5±0.2
F5	348±1.8	4.51±0.29	3.39±0.49	0.57±0.13	99±4	93.32±0.51	97.4±0.4
F6	350±2.2	4.57±0.33	3.43±0.51	0.58±0.11	87±4	95.25±0.67	98.3±0.7
F7	349±1.3	4.48±0.31	3.32±0.59	0.33±0.21	88±3	89.62±0.70	94.8±0.8
F8	351±2.6	4.55±0.22	3.37±0.47	0.56±0.23	107±6	91.48±0.56	99.8±0.4
F9	350±2.2	4.57±0.37	3.44±.29	0.38±0.16	103±4	94.58±66	98.7±0.3
F10	351±2.2	4.48±0.33	3.47±0.26	0.39±0.17	126±5	98.31±0.66	95.3±0.8
F11	352± 2.6	4.58±0.29	3.49±0.43	0.36±0.14	107±6	89.48±0.32	98.6±0.4
F12	351±1.3	4.73±0.31	3.52±0.57	0.47±0.27	102±6	95.58±0.75	97.1±0.7
F13	351±2.2	4.54±0.22	3.43±0.52	0.49±0.19	94±5	97.98±0.48	99.5±0.2
F14	353±1.8	4.61±0.37	3.49±0.47	0.44±0.22	103±4	93.32±0.71	97.4±0.5
F15	350±1.8	4.47±0.31	3.50±0.43	0.48±0.17	101±4	96.25±0.37	98.3±0.7
F16	351±0.9	4.39±1.12	3.46±0.52	0.51±0.21	96±3	95.62±0.30	97.8±0.8
F17	349±1.3	4.47±1.17	3.57±0.27	0.50±0.19	92±5	91.48±0.96	98.8±0.4
F18	350±1.5	4.54±0.24	3.52±0.22	0.48±0.27	104±4	97.58±0.86	97.7±0.4
F19	351±1.8	4.56±1.99	3.50±0.23	0.47±0.21	93±6	89.91±0.96	95.4±0.7
F20	349± 1.6	4.61±0.26	3.51±0.12	0.51±0.12	108±3	94.48±0.52	98.3±0.5
F21	350±0.9	4.58±0135	3.46±0.41	0.53±0.09	94±2	96.58±0.45	97.1±1.6
F22	352±1.9	4.63±0.34	3.46±0.33	0.57±0.27	107±5	96.98±048	98.5±0.26
F23	351±1.8	4.64±0.21	3.47±0.49	0.54±0.13	103±5	88.32±0.51	94.4±0.4
F24	350±2.6	4.56±0.33	3.45±0.41	0.51±0.17	99±4	95.25±0.67	96.3±0.4
F25	349±1.3	4.47±0.38	3.32±0.39	0.43±0.31	101±4	98.62±0.70	97.8±0.5
F26	351±2.7	4.52±0.26	3.57±0.27	0.56±0.23	103±5	96.48±0.56	96.8±0.3
F27	352±2.2	4.57±0.37	3.44±.29	0.48±0.36	104±4	97.58±66	95.7±0.5
F28	349± 1.6	4.61±0.26	3.51±0.12	0.51±0.12	98±3	94.48±0.52	98.3±0.5
F29	350±1.5	4.54±0.24	3.52±0.22	0.48±0.27	104±4	97.58±0.86	97.7±0.4
F30	353±1.8	4.61±0.37	3.49±0.47	0.44±0.22	103±4	93.32±0.71	97.4±0.5

Evaluation of tablets

Weight variation:

The total weight of each formulation was not maintained constant however; the weight variation of the tablets was within the permissible limits of 5%, as specified. (Table 7).

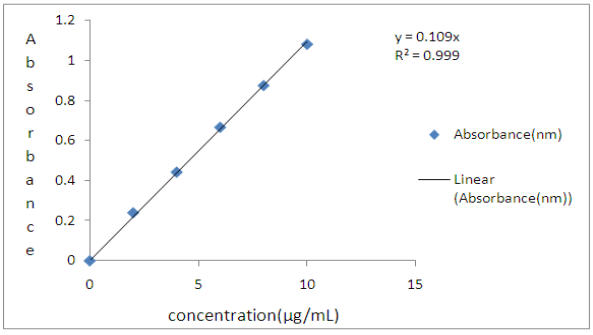

Fig. 1: Standard graph of deferasirox in pH 6.8 buffer

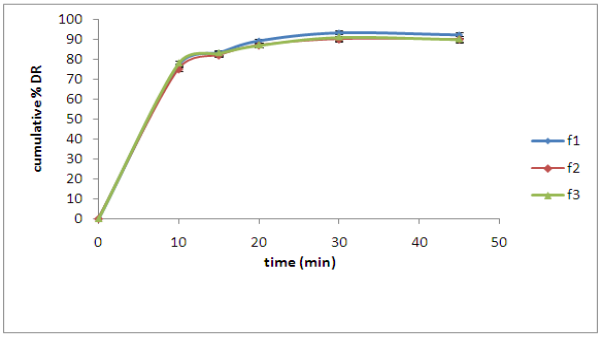

Fig. 2: Comparison of dissolution profile for F1, F2, F3 batches

In-vitro dissolution study of formulations F1, F2 and F3 batches showed drug release of 87%, 93%, 91% within 30 min. F2 batch shown good dissolution profile (Figure 2). F2 batch contain 4% of crospovidone as superdisintegrant and Lactose as diluent.

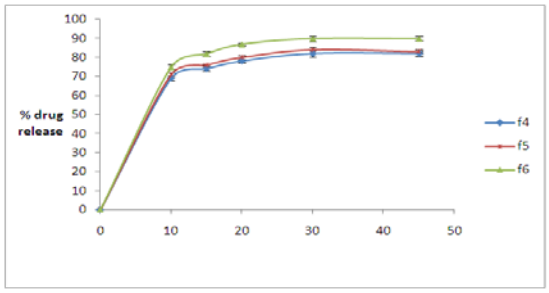

Fig. 3: Comparison of dissolution profile for F4, F5, F6 batches

In-vitro dissolution study of formulations F4, F5 and F6 batches showed drug release of 82%, 84% and 90% within 30 min. Among these formulations F6 batch shown good dissolution profile (Figure 3). F6 batch contain 6% of Croscarmellose as superdisintegrant and Lactose as diluent.

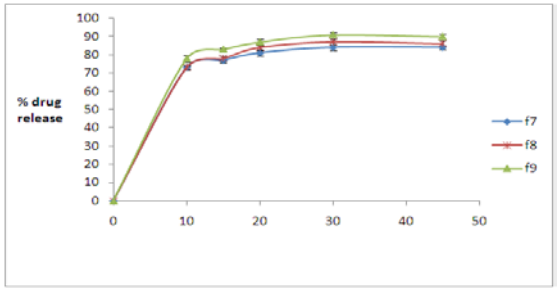

Fig. 4: Comparison of dissolution profile for F7, F8, F9 batches

In-vitro dissolution study of formulations F7, F8 and F9 batches showed drug release of 84%, 87% and 91% within 30 min. Among these formulations F9 batch shown good dissolution property (Figure 4). F9 batch contain 6% of sodium starch glycolate as superdisintegrant and lactose as diluent.

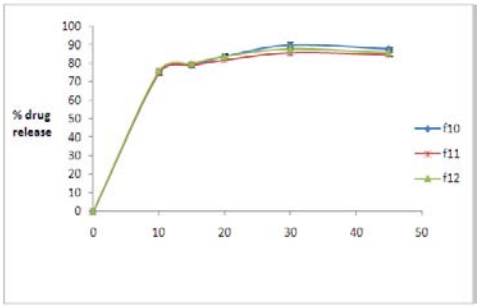

Fig. 5: Comparison of dissolution profile for F10, F11, F12 batches

In-vitro dissolution study of formulations F10, F11 and F12 batches showed drug release of 82%, 85% and 90% within 30 min. Among these formulations F12 batch shown good dissolution profile (Figure 5). F12 batch contain 6% of crospovidone as superdisintegrant and mannitol as diluent.

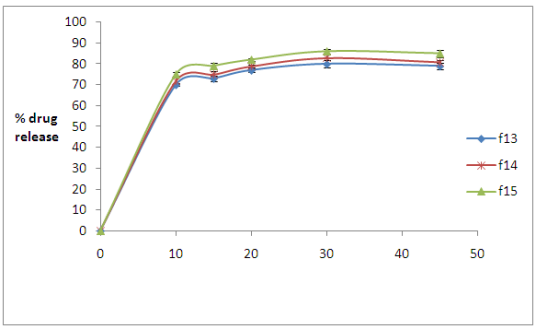

Fig. 6: Comparison of dissolution profile for F13, F14, F15 batches

In-vitro dissolution study of formulations F13, F14 and F15 batches showed drug release of 80%, 83% and 86% within 30 min. Among these formulations F15 batch shown good dissolution property (Figure 6). F15 batch contain 6% of croscarmellose as superdisintegrant and mannitol as diluent.

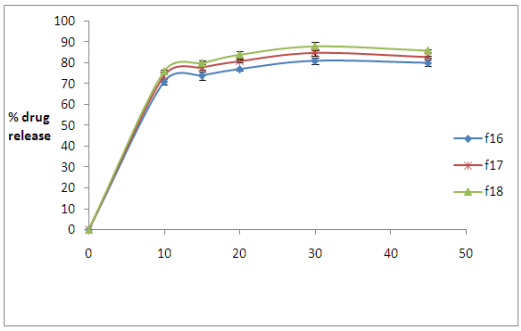

Fig. 7: Comparison of dissolution profile for F16, F17, F18 batches

In-vitro dissolution study of formulations F16, F17 and F18 batches showed drug release of 81%, 85% and 88% within 30 min. Among these formulations F18 batch shown good dissolution profile (Figure 7). F18 batch contain 6% of sodium starch glycolate as superdisintegrant and mannitol as diluent.

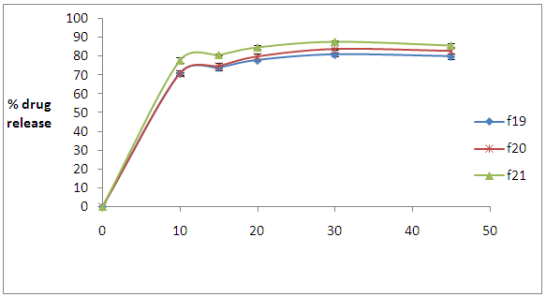

Fig. 8: Comparison of dissolution profile for F19, F20, F21 batches

In-vitro dissolution study of formulations F19, F20 and F21 batches showed drug release of 81%, 84% and 88% within 30 min. Among these formulations F21 batch shown good dissolution property (Figure 8). F21 batch contain 6% of crospovidone as superdisintegrant and Micro crystalline cellulose as diluent.

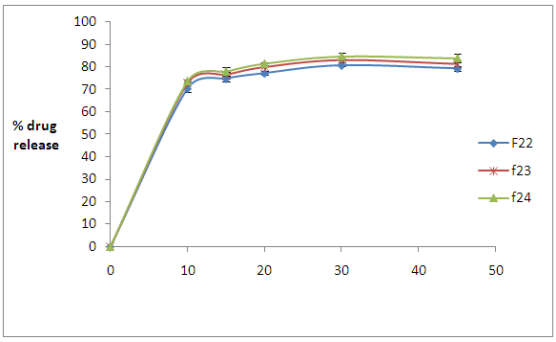

Fig. 9: Comparison of dissolution profile for F22, F23, F24 batches

In-vitro dissolution study of formulations F22, F23 and F24 batches showed drug release of 80%, 82% and 84% within 30 min. Among these formulations F24 batch showed good dissolution property (Figure 9). F24 batch contain 6% of croscarmellose as superdisintegrant and Micro crystalline cellulose as diluent.

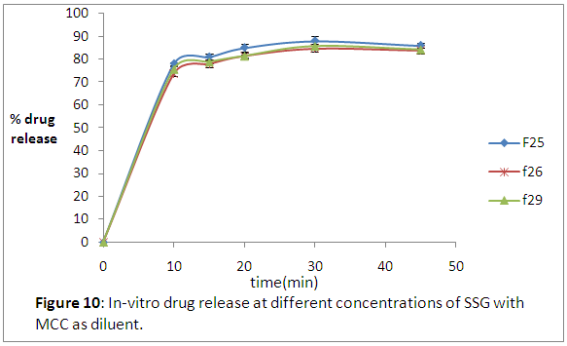

Figure 10: In-vitro drug release at different concentrations of SSG with MCC as diluent.

Fig. 10: Comparison of dissolution profile for F25, F26, F27 batches

In-vitro dissolution study of formulations F25, F26 and F27 batches showed drug release of 80%, 82% and 85% within 30 min. Among these formulations F27 batch showed good dissolution property (Figure 10). F27 batch contain 6% of sodium starch glycolate as superdisintegrant and Micro crystalline cellulose as diluent.

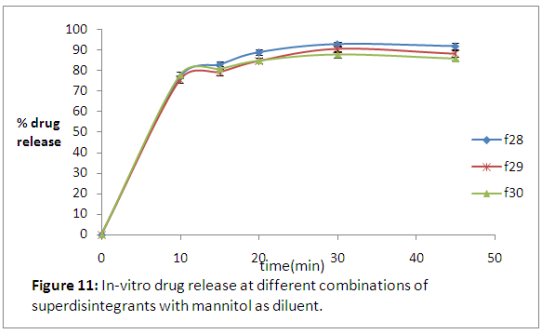

Figure 11: In-vitro drug release at different combinations of superdisintegrants with mannitol as diluent.

Fig. 11: Comparison of dissolution profile for F28, F29, F30 batches

In-vitro dissolution study of formulations F28, F29 and F30 batches showed drug release of 83%, 85% and 81% within 30 min. Among these formulations F29 batch showed good dissolution property (Figure 11). F29 batch contain 4% of crospovidone and 4% of sodium starch glycolate as superdisintegrants in combination and mannitol as diluent.

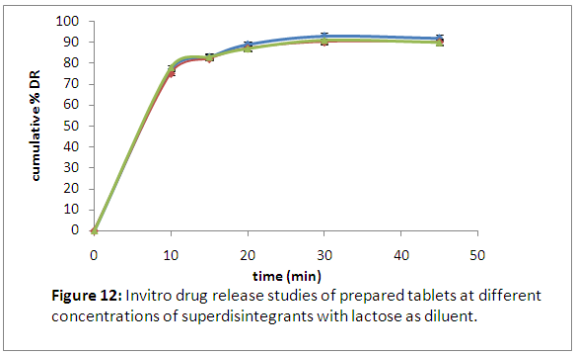

Figure 12: Invitro drug release studies of prepared tablets at different concentrations of superdisintegrants with lactose as diluent.

Fig. 12: Comparison of dissolution profile for F2, F6, F9 batches containing lactose as diluent.

In-vitro dissolution study of formulation F2 batch release the drug 93% within 30 min and other batches showed (Figure 12) less percentage of drug release than F2 batch. F2, F6 and F7 batches contain lactose as diluent but vary in different concentrations of different superdisintegrants.

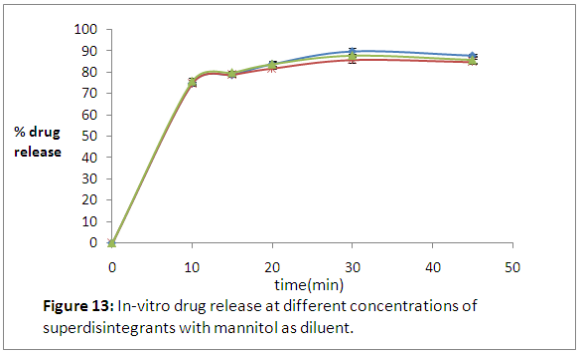

Figure 13: In-vitro drug release at different concentrations of superdisintegrants with mannitol as diluent.

Fig. 13: Comparison of dissolution profile for F12, F15, F18 batches containing mannitol as diluent.

In-vitro dissolution study of formulation F12 batch release the drug 90% within 30 min and other batches showed (Figure 13) less percentage of drug release than F12 batch. F12, F15 and F18 batches contain mannitol as diluent but vary in different concentrations of different superdisintegrants.

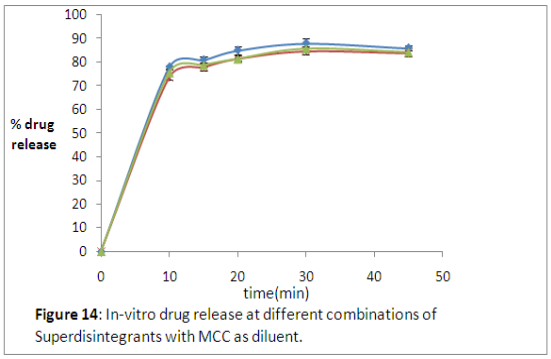

Figure 14: In-vitro drug release at different combinations of Superdisintegrants with MCC as diluent.

Fig. 14: Comparison of dissolution profile for F21, F24, F27 batches containing MCC as diluent.

In-vitro dissolution studies of formulation F21 batch release the drug 88% within 30 min and other batches showed (Figure 14) less percentage of drug release than F21 batch. F21, F24 and F27 batches contain MCC as diluent but vary in different concentrations of different superdisintegrants.

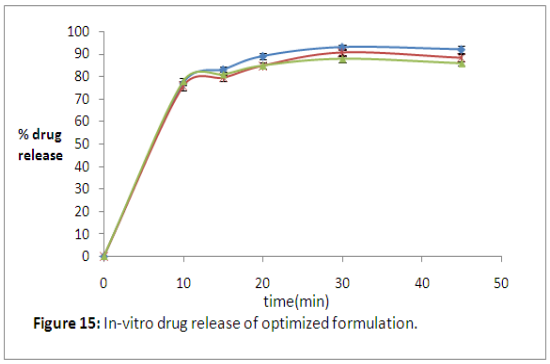

Figure 15: In-vitro drug release of optimized formulation.

Fig. 15: Comparison of dissolution of F2, F12, F21 batches.

In-vitro dissolution study of formulation F2 batch containing superdisintegrant crospovidone release the drug 93% within 30 min and other batches showed (Figure 15) less percentage of drug release than F2 batch.

It clearly shows due to the superdisintegrant – crospovidone (4%) and it seems to be the best. The reason is its highly porous structure and water wicking mechanism into porous network of tablet and hence increases in concentration of crospovidone accounts for rapid drug release.

Among the formulations (F1-F30), F2 batch has shown good release of drug within 30 min. F2 batch contain crospovidone as superdisintegrant and lactose as diluent. Compared with other superdisintegrants, crospovidone has good disintegration property which enables good dissolution of the formulation, whereas croscarmellose and SSG have delayed disintegration, due to their tendency to gel more than crospovidone. On the other side lactose and mannitol have good solubility than microcrystalline cellulose. Compared to mannitol, lactose has slight increase in solubility, so it enables easy and fast release of the drug. Whereas microcrystalline cellulose is insoluble in water, which forms compact tablet, hence slow release of drug.

So, it is assumed that 4% crospovidone with lactose as diluent is optimized in which it shown a drug release of 93% compared with other batches.

Fourier transform infrared spectroscopy

The IR spectra of pure deferasirox drug showed the characteristic absorption bands are as follows: COO- at 1680 cm-1, aliphatic triazolidine stretching at 3085 cm-1, O-H stretching of aromatic ring at 1351 cm-1, carboxyl keto group showed absorption band at 1607 cm-1, and strong bending mode at 900-650 cm-1(Spectra 1). No drug-polymer interaction was observed in the FTIR spectra of the powder mixture of optimized formulation (Spectra 2) since the absorption peaks of the drug still could be detected in the mixture.

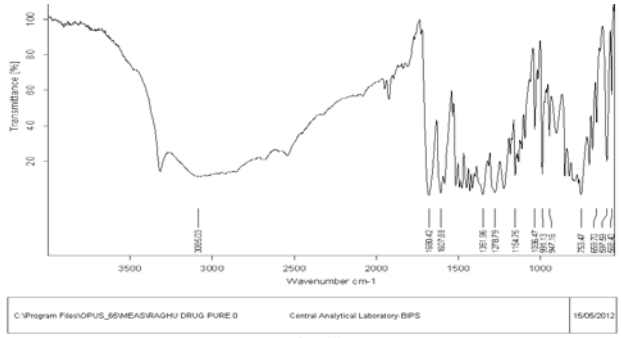

Fig. 16: FTIR spectrum of Deferasirox

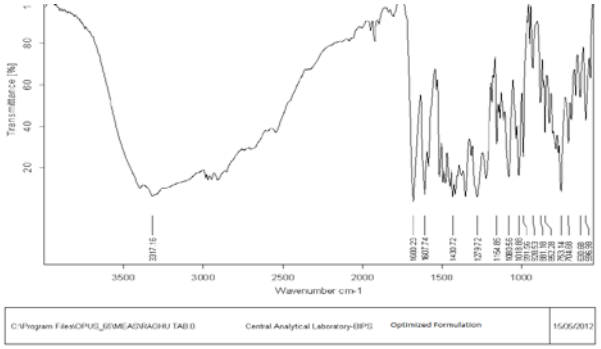

Fig. 17: FTIR spectrum of Optimized formulation

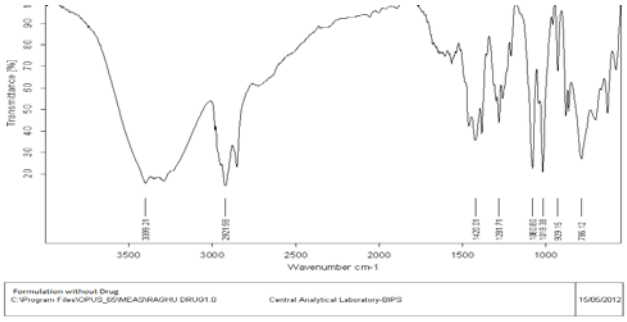

Fig. 18: FTIR spectrum of Placebo

CONCLUSION

Deferasirox fast disintegrating tablets were successfully formulated by employing direct compression method and found to show the significant level of drug release. From the *in-vitro* dissolution studies the formulation F2 were found to be better formulations and the dissolution efficiency was increased. FTIR study showed that there is no interaction between the drug and excipients. In conclusion, development of fast disintegrating tablets using superdisintegrants is able to give rapid drug delivery and there by rapid onset of action.

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ABBREVIATIONS

CCS: Croscarmellose sodium, SSG: Sodium Starch Glycolate, CP: Crospovidone, H: Hour, mg: Milligram, min: Minute, mL: Milliliter, N: Normality, rpm: Revolution per minute, Sec: Second, USP: United States of Pharmacopoeia, UV: Ultraviolet, Wt.: Weight, w/w: Weight by weight, mcg: Microgram, %: Percentage, Meq: Milli equilvalent, Lit:Litre, FDT: Fast disintegrating tablets, MD: mouth dissolving tablet, WHO: World health organization, FT-IR: Fourier Transform Infra-Red,

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