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Formulation and invitro evaluation of deferasirox oral suspension

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ABSTRACT

In present work an attempt has been made to prepare Deferasirox dispersible tablets with increased rate of dissolution may leads to increase bioavailability. In present work Deferasirox dispersible tablets prepared by using different superdisintegrants[8] by direct compression method. The tablets were evaluated for various parameters like weight variation, hardness, friability, *in vitro* disigration time, drug-polymer interaction, drug content water absorption ratio, wetting time, *in vitro* drug release, FTIR studies and short term stability studies. drug content uniformity was in between 98.1 to 101.0%, FTIR study showed that there was no drug interaction with formulation additives of the tablet, short term stability studies of the formulations indicated that there are no significant change in hardness, friability, drug content and *in vitro* drug release. Best formulation was compared with that of the innovator F8 and F9 were found complying with the innovator but due to lower SLS concentration in F9 formulation it is the best formulation.

Keywords: Deferasirox, Dispersible Tablets and Superdisintegrants.

INTRODUCTION[1, 2]

Chelators are small molecules that bind very tightly to metal ions. Some chelators are the molecules that can be easily manufactured[1] (e.g. ethylene diamine tetra acetic acid; EDTA). The other chelators are complex proteins made by living organisms[3] (e.g. transferrin). The key property shared by all chelators is that the metal ion bound to the chelator is chemically inert. Consequently, one of the important roles of chelators is to detoxify metal ions and prevent poisoning.

AIM AND OBJECTIVE

The objective of present study is to design and develop a stable solid oral dosage form of Deferasirox dispersible tablets[4] to deliver with optimum concentration of drug at desired site at specific time comparable to the innovator product with better stability, high production feasibility, and excellent patient compatibility[10].

1. Pre-formulation studies of excipients and their compatibility with the API.
2. Innovator product evaluation.
3. Development of various formulations and preparation of dispersible tablets by
4. Direct compression technique
5. Selection and optimization of the best formulation.
6. Comparison of the optimized formulation with the innovator product.
7. To perform stability studies on the most satisfactory formulation as per ICH guidelines

METHODOLOGY

Formulation development of deferasirox dispersible tablets

Direct compression method

Table 1: Formula for F-1, F-2, F-3, F-4,F-5, F-6, F-7, F-8, F-9

S.No	Ingredient	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
1	Deferasirox	250	250	250	250	250	250	250	250	250
2	Aerosil	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
3	Croscarmellose Sodium	25	50	25	25	25	25	25	50	50
4	MCC PH101	47.5	22.5	45	43.75	42.5	40	37.5	12.5	15
5	Starch 1500	25	25	25	25	25	25	25	25	25
6	Mannitol	125	125	125	125	125	125	125	125	125
7	SLS	-	-	2.5	3.75	5	7.5	10	10	7.5
8	Aspartame	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
9	Magnesium stearate	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
	Total weight	500	500	500	500	500	500	500	500	500

Procedure for Formulation

API, Starch 1500, Mannitol, SLS, Aspartame, Croscarmellose Sodium, MCC PH 101[2] were weighed and mixed for 2 mins.The above mixture was passed through #40mesh.Then the above blend is pre lubricated using Aerosil for 5mins and then lubricated with Magnesium stearate in blender for 2 mins.Then finally the lubricated blend was compressed using 12 mm round flat punches[5,6].

RESULTS AND DISCUSSION

Pre-formulation studies

Table 2: Drug-excipient compatibility studies

S.No	Ingredients	Ratio	Description		
			Initial	55°C (2 weeks)	40±2°C /75±5 % RH (4 weeks)
1	API	1	Off white	No change	No change
2	Mannitol	1	Off white	No change	No change
3	Croscarmellose Sodium	1	White	No change	No change
4	Starch 1500	1	White	No change	No change
5	MCC PH 101	1	Off white	No change	No change
6	SLS	1	White	No change	No change
7	Aerosil	1	White	No change	No change
8	Magnesium stearate	1	White	No change	No change
9	Aspartame	1	Off white	No change	No change

10	API+Croscarmellose sodium	5:1	Off white	No change	No change
11	API+ Starch 1500	5:1	Off white	No change	No change
12	API+ MCC PH 101	1:5	Off white	No change	No change
13	API+ SLS	5:1	Off white	No change	No change
14	API+ Aerosil	5:1	Off white	No change	No change
15	API+ Magnesium stearate	5:1	Off white	No change	No change

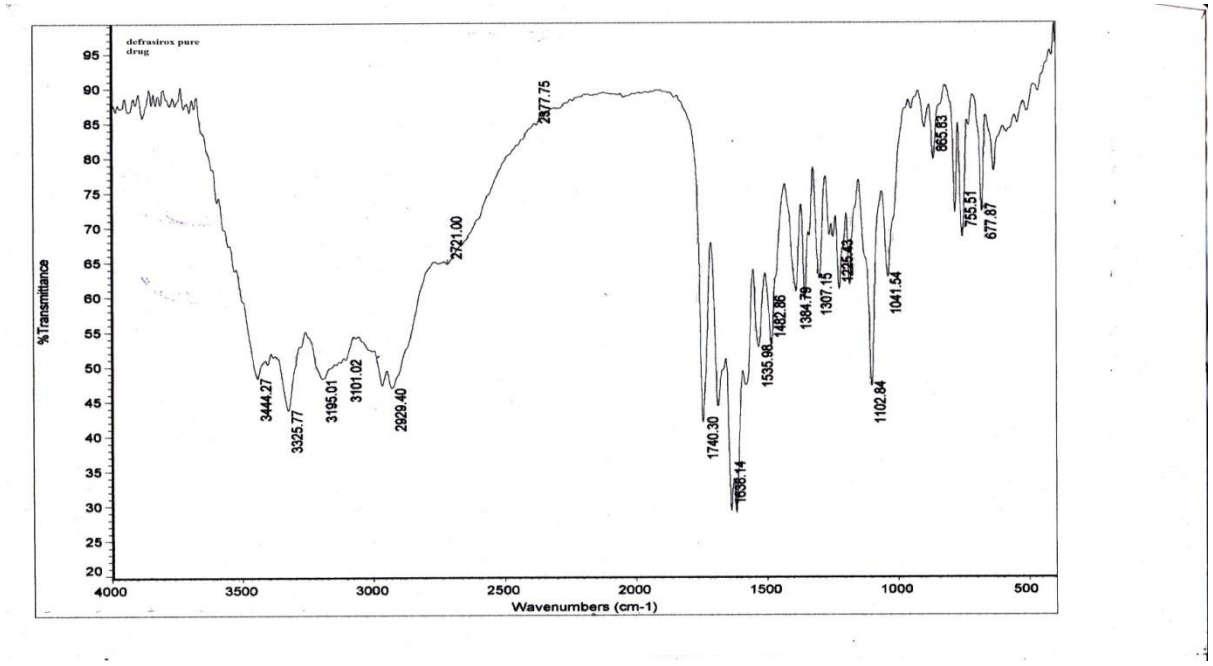

Fig No.1 FTIR of defrasirox pure drug

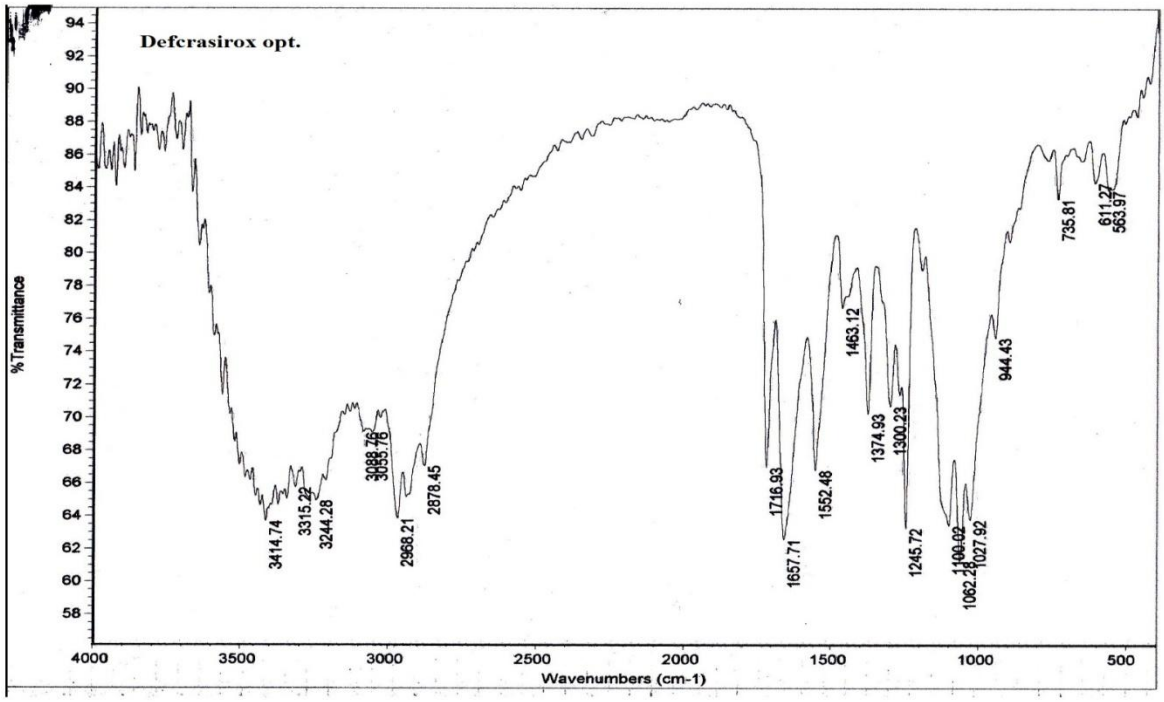

Fig No.2 FTIR of defrasiroxOptimised formulation

Table 3:Pre-compression parameters for formulations F-1 to F-9

Formula	Angle of repose	Compressibility Index (%)	Hausner ratio
F-1	25.80	20.40	1.06
F-2	20.32	20.26	1.03
F-3	25.70	20.74	1.02
F-4	24.28	20.20	1.13
F-5	22.16	18.23	1.15
F-6	20.34	17.50	1.11
F-7	26.59	13.00	1.15
F-8	25.26	12.26	1.14
F-9	25.12	12.44	1.13

Table 4:Post-compression parameters for formulations F-1 to F-9

Formula	Avg.weight (mg)	Thickness (mm)	Hardness (kp)	Friability (%)	Disintegration time (sec)	Assay (%)
F-1	502.6	3.97	5.02	0.28	29	99.8
F-2	504.1	3.52	5.13	0.29	38	98.3
F-3	497.2	3.31	5.48	0.22	52	101.0
F-4	501.0	3.27	5.52	0.29	59	99.5
F-5	505.7	3.60	5.44	0.20	63	100.7
F-6	503.0	3.38	5.79	0.21	51	98.1
F-7	502.0	3.36	5.85	0.23	32	99.7
F-8	503.4	3.43	5.80	0.23	35	100.2
F-9	**503.0**	**3.41**	**5.89**	**0.20**	**34**	**99.98**

Table 5: Dissolution profiles of different formulations (F-1 to F-9)

Sampling Time (minutes)	Cumulative Percentage Drug Release								
	F-1	**F-2**	**F-3**	**F-4**	**F-5**	**F-6**	**F-7**	**F-8**	**F-9**
10	22.5	30.7	29.6	34.9	36.8	39.6	48.4	67.2	**68.0**
20	38.0	36.4	43.3	40.0	50.2	50.5	54.3	84.8	**85.1**
30	53.6	58.5	60.1	65.5	69.3	77.7	77.1	98.3	**98.6**
45	58.8	60.9	67.4	74.3	78.6	83.4	84.3	98.2	**98.4**

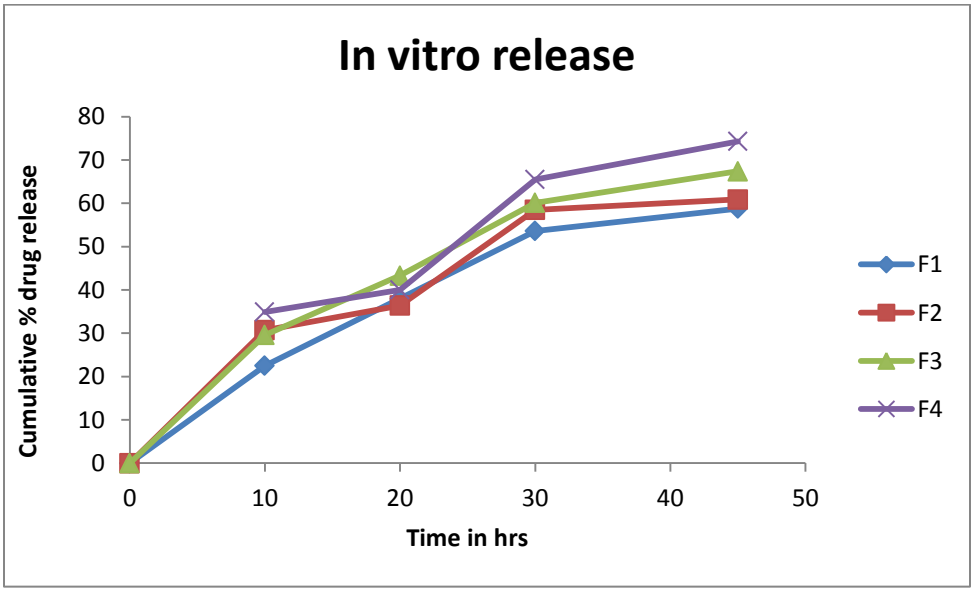

Figure 3: Dissolution profile of formulations 1-4

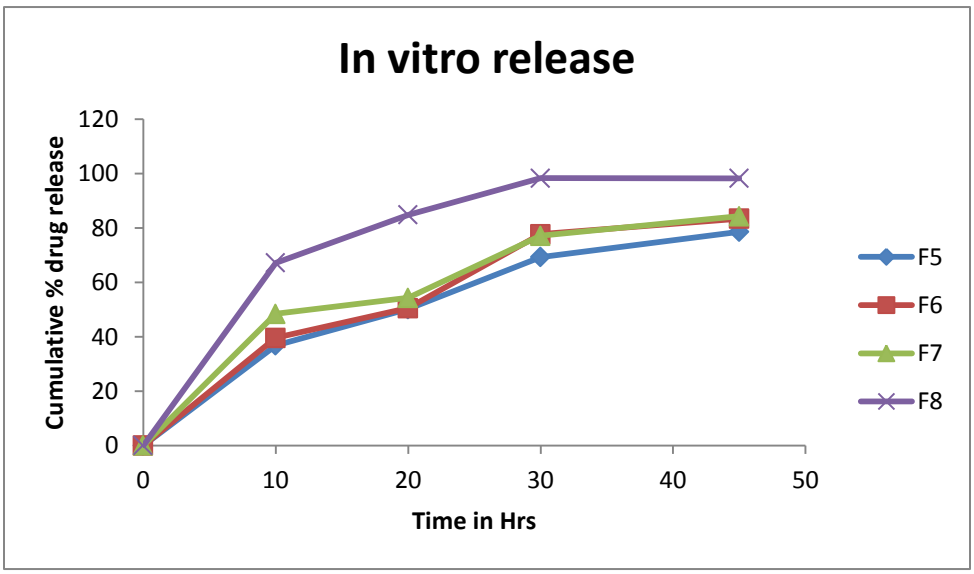

Figure 4: Dissolution profile of formulations 5-8

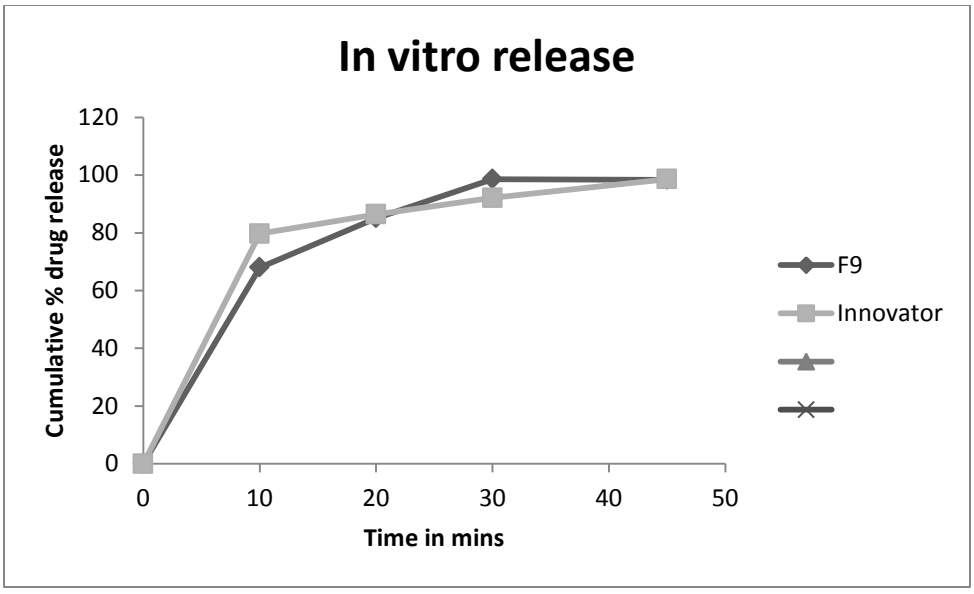

Figure 5: Dissolution profile of formulations 9 and innovator

Stability data

Table 6: Physical and chemical parameters of Deferasirox dispersible tablets (F-9) after 1st and 3rdmonthat 40±2°C /75±5 %RH

Parameter	Initial	1 Month	3 Month
Description	Light orange coloured round shaped uncoated tablets	No change	No change
Avg.wt (mg)	503.0	503.2	503.4
Hardness (kp)	4.89	4.83	4.77
Thickness (mm)	4.41	4.48	4.53
Friability (%)	0.20	0.23	0.26
Assay (%)	99.98	100.5	99.47

Table 7: Dissolution profiles of Deferasirox dispersible tablets (F-9) after 1st and 3rd month at 40±2°C /75±5 %RH

Time interval (min)	Cumulative percentage drug release		
	Initial	1 Month	3 Month
10	78.0	78.12	78.4
20	85.1	84.3	84.7
30	97.4	97.1	96.6
45	97.3	97.1	96.5

Table 8:Physical and chemical parameters of Deferasirox dispersible tablets (F-9) after 1st and 3rdmonthat 40±2°C /75±5 %RH

Parameter	Initial	1 Month	3 Month
Description	Light orange coloured round shaped uncoated tablets	No change	No change
Avg.wt (mg)	503.0	503.2	503.1
Hardness (kp)	4.89	4.86	4.82
Thickness (mm)	4.41	4.50	4.54
Friability (%)	0.20	0.24	0.23
Assay (%)	99.98	100.2	99.41

Table 9: Dissolution profiles of Deferasirox dispersible tablets (F-9) after 1st and 3rd month at 40±2°C/75±5 %RH

Time interval	Cumulative percentage drug release		
(min)	Initial	1 Month	3 Month
10	78.0	78.4	78.7
20	85.1	85.6	84.9
30	97.4	97	96.4
45	97.3	96.9	96.3

DISCUSSION

The tablet prepared by direct compression method passes weight variation was found in the range 497 to 504 mg which is below 5%, hardness 50.2 to 5.89Kg /cm2, percentage friability of 0.20 to 0.29 %, *in vitro* disintegration time of 29 to 63 secs, drug content uniformity was in between 98.1 to 101.0%, The formulation f9 was optimized and showing 98.4% drug release in 45 min

CONCLUSION

The present investigation was undertaken to formulate Deferasirox into dispersible tablet for the treatment of chronic iron overload. For the development and formulation of dispersible tablets, wet granulation and direct compression techniques were carried out with combination of various approved excipients. All the experimental formulation batches have been subjected to various evaluation parameters viz, average weight, thickness, hardness, friability, disintegration, uniformity of dispersion, dissolution studies, water content and assay. **Formulation F- 1-9** were carried out by direct compression method using ingredients such as Mannitol, Croscarmellose sodium, MCC PH 101, Starch 1500, SLS, Aerosil and Magnesium stearate. Here poor flow property was observed, hardness and friability values were also not satisfactory. The disintegration time were found to be 36 sec respectively. The percentage of drug release of F8 and F9 were found to be complying with that of the innovator product values. Of both F8 and F9, F9 has lower percentage of SLS so it is taken as best formulation.

REFERENCES

[1]. *Keberle H, The biochemistry of deferoxamine and its relation to iron metabolism*. ***Ann NY Acad Sci****. 1964; 119:758-775*.

[2]. *Nash R.A, Metals in medicine*. ***Alternative Therapies in Health and Medicine****. 2005*; *11(4)*:*18-25*.

[3]. Mendes Al, Ferro A, Martin R, Non-classical hereditary haemochromatosis in Portugal: novel mutations identified in iron metabolism-related genes. ***Ann. Haematol***. 2009; 88(3):229-34.

[4]. *V.P*. Choudhry, Rahul Naithani, *Current Status of Iron Overload and Chelation* with *Deferasirox*. ***Indian J Pediatr***. *2007*; *74(8)*:*759-764.*
[5]. Lachman L, Liberman H, Kanig J, The Theory and Practice of Industrial Pharmacy, 3rd ed. Pg. no. 293-345, 346-373.
[6]. Aulton M, Pharmaceutics: The Science of Dosage Form Design, International Student Edition. Pg. no. 304-321, 347-668.
[7]. http://www.faqs.org/patents/app/20080312168
[8]. Reddy LH, Ghosh B, Rajneesh, Fast dissolving drug delivery systems: A Brief Overview. ***Indian J Pharm Sci***. Jul 2002; 64(4):331-336.
[9]. Sreenivas SA, Dandagi PM, Gadad AP, Godbloe AM, Hiremath SP, Mastiholimath VS, Orodispersible tablets: New-fangled drug delivery systems-A review. ***Indian J Pharm Educ Res***. Oct 2005; 39(4):177-81.
[10]. Brown D, Orally disintegrating tablets-taste over speed. ***Drug Delivery technol***. 2001; 3(6):58-61.
[11]. *Habib W, Khankari R, Hontz J, Fast-dissolving Drug Delivery Systems.* ***Critical*** **Reviews TM** ***Therapeutic Drug Carrier Systems.*** *2000*; 17(1): 61-72.
[12]. H. Seager, Drug Delivery Products and the Zydis Fast-Dissolving Dosage Form. ***Journal.Pharm.Pharmcol***. 1998; 50**:**375–385.
[13]. http://www.pharmpedia.com/Tablet:Manufacturing_methods/Granulation
[14]. Brahmeshwar Mishra , Mouth Dissolving Tablets I: An Overview of Formulation Technology. ***Sci Pharm***. 2009; 77: 309-326.