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Research Article

Formulation Development and Evaluation of Deferasirox dispersible tablets

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Abstract

Formulation development and evaluation of Deferasirox dispersible tablets focuses on designing a patient-friendly, orally administrable dosage form that ensures rapid dispersion, enhanced palatability, and consistent bioavailability. Deferasirox, a poorly water-soluble iron-chelating agent, requires formulation strategies such as the use of suitable superdisintegrants, wet granulation techniques, and solubilizing agents to improve its dissolution profile. The development process typically involves optimization of tablet hardness, friability, disintegration time, and uniformity of drug content to achieve robust mechanical strength while maintaining fast dispersion in water. Evaluation studies further include in-vitro dissolution testing, compatibility assessments, and stability studies to ensure long-term product performance. Overall, well-designed Deferasirox dispersible tablets provide an effective and convenient therapeutic option for pediatric and geriatric patients requiring chronic iron chelation therapy. The objective of the current study was to development optimize a oral disintegration tablets. Deferasirox is a rationally designed oral Iron chelator.

Keywords: Deferasirox, solubilizing agents, Evaluation, patients

INTRODUCTION

Dispersible tablets (DTs) are solid oral dosage forms designed to disintegrate and disperse rapidly in water before administration, providing an easily swallowable dispersion for adult, pediatric, and geriatric patients. They represent a significant advancement in patient-centric drug delivery, particularly for individuals with dysphagia, children who have difficulty swallowing conventional tablets, and patients requiring rapid onset of action. DTs combine the advantages of conventional tablets—accuracy, stability, and convenience—with improved patient compliance and ease of administration. [1,2]The pharmaceutical development of dispersible tablets encompasses pre-formulation studies, selection of excipients, formulation strategies, manufacturing processes, and rigorous evaluation parameters to ensure quality, safety, and efficacy.

Pre-Formulation Considerations [3,4]

The development of dispersible tablets begins with pre-formulation studies to understand the physicochemical and biopharmaceutical properties of the active pharmaceutical ingredient (API). Important parameters include solubility, stability, hygroscopicity, particle size, and compatibility with excipients. Poorly soluble drugs may require solubility-enhancing techniques such as solid dispersions, use of hydrophilic carriers, or incorporation of surfactants. Drug–excipient compatibility studies, often assessed by differential scanning calorimetry (DSC), infrared spectroscopy, and stability studies, help ensure that the combination remains stable during processing and shelf life. The selected API should ideally have a pleasant taste, but if bitterness is

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present, taste-masking strategies such as coating, complexation with ion-exchange resins, and sweeteners become essential to enhance patient acceptance.

Key Formulation Components

Formulating dispersible tablets requires a careful selection of excipients that facilitate rapid disintegration while maintaining adequate mechanical strength.

a. Superdisintegrants

Superdisintegrants are essential to ensure fast breakup of the tablet upon contact with water. Commonly used agents include:

- Cross-linked polyvinylpyrrolidone (Crospovidone)
- Croscarmellose sodium
- Sodium starch glycolate

These materials promote wicking, swelling, or deformation recovery mechanisms to achieve rapid dispersion, usually within 3 minutes as recommended by pharmacopeias.

b. Diluents / Fillers

Fillers provide bulk and help improve tablet texture. Widely used diluents include microcrystalline cellulose (MCC), lactose monohydrate, mannitol, and dextrose. Mannitol is particularly preferred due to its pleasant mouthfeel and cooling sensation.[5,6]

c. Binders

Binders such as povidone, starch paste, hydroxypropyl methylcellulose (HPMC), or pregelatinized starch ensure adequate cohesiveness during granulation and tablet compression, preventing capping or lamination.

d. Lubricants and Glidants

Lubricants like magnesium stearate, talc, or sodium stearyl fumarate reduce friction during tablet compression. However, excessive hydrophobic lubricants may delay dispersion, so optimized concentrations are critical.

e. Taste-masking and Organoleptic Agents

Flavoring agents (orange, strawberry), sweeteners (aspartame, sucralose, saccharin), and coloring agents are added to enhance palatability, especially for pediatric use.

Methods of Preparation of Dispersible Tablets

Several manufacturing techniques can be employed depending on the properties of the API and excipients.

a. Wet Granulation

Wet granulation is widely used due to its ability to enhance flow properties and ensure uniform distribution of API. The process involves:[7,8,9]

1. Mixing the drug with diluents.
2. Adding a binder solution to form a wet mass.
3. Passing the wet mass through sieves to form granules.
4. Drying and resizing the granules.
5. Blending with lubricants and superdisintegrants.
6. Compressing into tablets.

Wet granulation improves compressibility and reduces segregation but must be carefully controlled to avoid overwetting or loss of superdisintegrant activity.

b. Dry Granulation

Dry granulation is suitable for moisture- or heat-sensitive drugs. It involves slugging or roller compaction followed by milling and compression. Although it avoids exposure to water, it may not provide as rapid dispersion as wet granulation unless optimized.

c. Direct Compression

Direct compression is the most preferred technique for dispersible tablets due to simplicity, reduced processing steps, and cost-effectiveness. It requires excipients with excellent flow and

compressibility, such as spray-dried lactose, MCC, and specialized superdisintegrants. The direct compression method also minimizes variability and enhances tablet robustness.

d. Lyophilization / Freeze-Drying

Although primarily used for orally disintegrating tablets (ODTs), lyophilization can be applied to dispersible formulations requiring ultra-fast dispersion. The technique produces highly porous structures but is expensive and less suited for moisture-sensitive materials.

Evaluation of Dispersible Tablets

A series of evaluation tests ensure that dispersible tablets meet pharmacopeial standards:[5,6]

a. Appearance and Weight Variation

Tablets must be uniform and free of defects. Weight variation ensures dose accuracy.

b. Hardness and Friability

Hardness should be sufficient for mechanical stability but not so high as to retard dispersion. Friability is checked using a friabilator, with acceptable losses below 1%.

c. Wetting Time and Dispersion Time

Wetting time assesses how quickly water penetrates the tablet. Dispersion time—typically within 3 minutes according to IP and BP—is a critical quality attribute.

d. Disintegration Time

Disintegration tests confirm rapid breakup in water. For dispersible tablets, the time is generally < 180 seconds.

e. Drug Content Uniformity

Ensures uniform distribution of the API across all tablets.

f. In-Vitro Dissolution

Dissolution studies provide insights into drug release kinetics and ensure bioavailability comparable to conventional tablets or innovator products.

g. Stability Studies

Carried out under ICH guidelines to evaluate physical and chemical stability, including moisture uptake, taste integrity, and mechanical strength.

Advantages of Dispersible Tablets

- Improved patient compliance
- Rapid onset of action
- Easy administration without swallowing
- Suitable for pediatric and geriatric populations
- Accurate dosing compared to liquid formulations
- Improved solubility and bioavailability for certain drugs

Applications

Dispersible tablets are widely used in antibiotics (amoxicillin, cefixime), NSAIDs (ibuprofen, diclofenac), antimalarials (artesunate), antihistamines, vitamins, and iron chelators. Their adaptability makes them valuable across therapeutic areas requiring user-friendly oral formulations.[10,11]]

MATERIAL AND METHODS

- Pre formulation studies of excipients and their compatibility with the API. Innovator product evaluation.
- Development of various formulations and preparation of dispersible tablets by Direct compression method & Wet granulation technique
- Selection and optimization of the best formulation.
- Comparision of the optimized formulation with the innovator product.
- To perform stability studies on the most satisfactory formulation as per ICH guidelines.[12,13,14]

I. Pre-compression parameters:

- Angle of repose
- Bulk density
- Tapped density
- Hausner's ratio
- Compatibility study

AI. Post-compression parameters:

- Hardness uniformity
- Uniformity of thickness
- Friability test
- Weight uniformity test
- Drug content uniformity
- Wetting time
- *In vitro* dispersion time
- *In vitro* disintegration time
- *In vitro* dissolution studies
- Final comparisons between evaluated results of direct compression.

RESULTS AND DISCUSSION

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 was carried out by direct compression method using ingredients such as lactose mono hydrate, Crospovidone XL, MCC pH 102, Starch 1500, SLS, Aerosil and Magnesium stearate. Here poor flow property was observed, hardness and friability values were also not satisfactory. The disintegration time and dispersion time were found to be 36 and 71 sec respectively. The percentage of drug release was 88.8% (in 45 mins) and it does not comply with the innovator product. So, we planned to forward the next batch using wet granulation method.

Formulation F-2 was carried out by wet granulation technique. Here Povidone K30 was used as a binder which was dispersed in water to make a solution. The other excipients are same as the previous formula except MCC pH 102 which is replaced by MCC pH101 and starch (excluding from the formulation). In this formula both the binder and superdisintegrant concentrations were taken as 25mg/tab each. Here hardness was found to be less and the friability value does not comply with the specifications. The disintegration time and dispersion time were found to be 40 and 63sec respectively. The percentage of drug release was 87.9% (in 45mins) and it was found to be less when to compared with the innovator product. So, we planned to forward the next batch by increasing both the binder and superdisintegrant concentrations.

Formulation F-3 was carried out by using the same excipients as that of the previous formula. Here binder and super disintegrant concentrations were raised to 45mg/tab and 30mg/tab respectively. Improvement in the hardness was observed. The disintegration time (62 sec) and dispersion time (118 sec) does not comply with the innovator product.

The percentage of drug release was found to be 86.4 %(in 45 mins). So, for better disintegration the next batch was planned by increasing super disintegration concentration.

Formulation F-4 was carried out by using the same excipients as that of the previous batch. Here the binder was same as the previous batch but the superdisintegrant concentration was raised to 35mg/tab. Then also the disintegration and dispersion of the compressed tablets was slightly poor i.e. a small amount of substance was retained on the sieve while passing through sieve no.22. It indicates that this batch also fails the specific test for dispersible tablets. The disintegration time and dispersion time were found to be 58 and 109sec respectively. The percentage of drug release was 89.3 %(in 45mins) and it does not comply with the innovator product. So, the next batch was carried out by changing the formula.

Formulation F-5 was made by using a new formula i.e. hydroxyl propyl cellulose (L-HPC_LH11), SSG, Magnesium stearate, Talc and SSF. The binder solution was prepared by dispersing Povidone K30 and Tween *0. The disintegration time and dispersion time were 67 sec and 125 sec respectively. Even though SSG was used as a superdisintegrant, poor dispersion was occurred and the residue was retained on the sieve when it was passed through sieve no.22. The percentage of drug release was found to 73.6 %(in 45 mins) and it does not comply with the innovator product. So, in order to get a better dispersion the next batch was planned by incorporating starch 1500 and increasing the concentration of superdisintegrant.

Formulation F-6 was made by using the same formula as that of F-4 and additionally starch 1500 was added. Here the superdisintegrant concentration was raised to 50mg/tab. The disintegration time and dispersion time were found to be 49 and 92 sec respectively. Even though starch 1500 was added to the formula for better dispersion still amount of residue remained on the sieve while passing. The percentage of drug release was 91.4% (in 45 mins) and it does not comply with the innovator product. So, next batch was planned by excluded lactose monohydrate and increasing the concentration of superdisintegrant.

Formulation F-7 was made by using the same formula of the previous batch by excluding lactose monohydrate and the concentration of superdisintegrant was increased to 100mg/tab. The disintegration time (32sec) and the dispersion time (65 sec) were found to be satisfactory and the percentage of drug release (97.2%) also improved by comparing with the previous batches and it was found to match with the innovator product. Here the dispersed mixture passed freely from sieve without any residue. So, the next batch was performed by adding colour, flavor and sweetener for better taste and appearance of the tablet.

Formulation F-8 was performed by using the same formula of the previous batch by including colour, flavor and sweetener. This batch was taken to improve the appearance as well as for better acceptability. The disintegration time (35sec), dispersion time (67 sec) and the percentage of drug release(98.3% in 45mins) were found to be satisfactory and it matches with innovator product(ASUNRA). So, the next batch performed by increasing the batch size to check the reproducibility.

Formulation F-9 was performed by using the same formula of the previous batch by increasing the batch size for reproducibility. The disintegration time (34sec), dispersion time (62sec) and percentage of drug release (97.4% in 45 mins) matches with that of the innovator (ASUNRA). Then the formulated tablets were loaded for stability as per ICH guidelines.

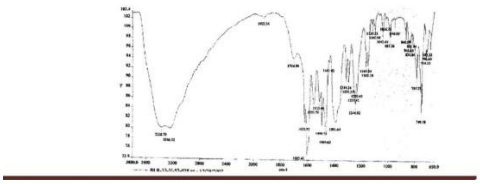

Figure1:FTIR specta of deferasirox

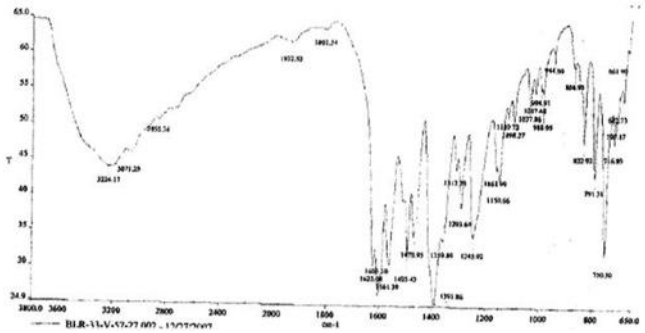

Figure2: FTIR sprctra of deferasirox and polymers

HPLC method:

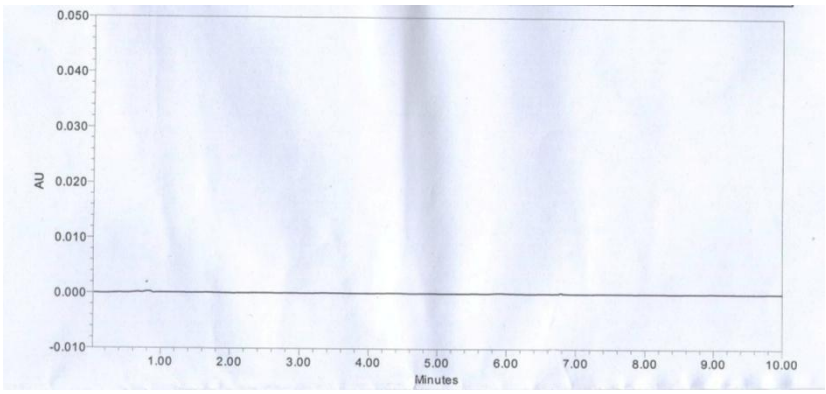

Figure3:Sample name deferasirox assay in Blank

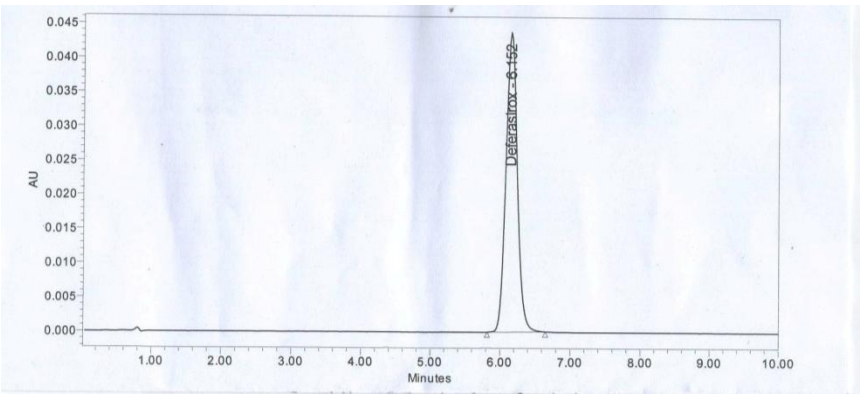

Figure4.:Standard graph

Table no1 .Assay standard:

Peak name	Via l	RTRatio	RT	Area a	% area t	Height	USP	Tailing	USP
Deferasiro	3	2	6.15	46934	100.0	43872	1.14	6879	0

Assay of deferasirox sample:

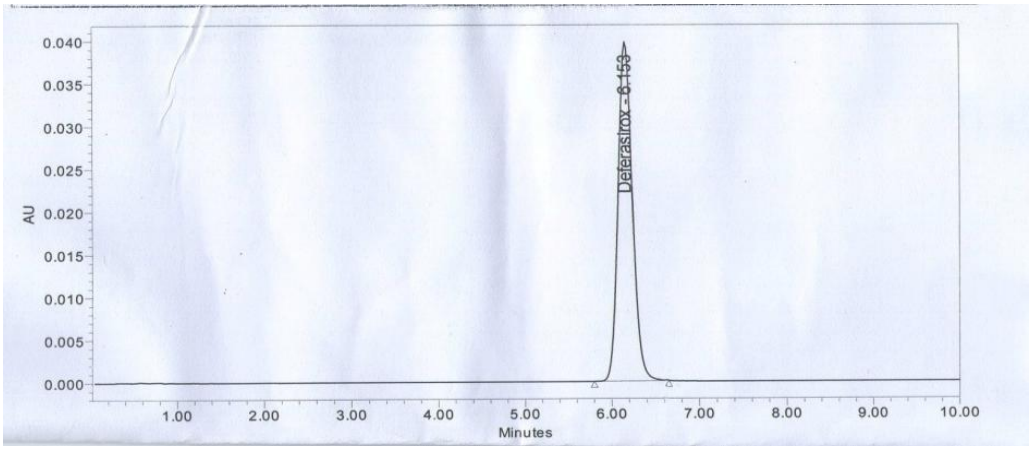

Figure5 :Sample of deferasirox

Table no2 :Assay of deferasirox in sample:

Peak name	Vial	RT	Ratio RT	Area	% area	Height	USP Tailing	USP Plate	USP Resol
Deferasirox	4	3	6.15	49868	100.00	39784	1.13	6899	0

Table 3: Disintegration time, Dispersion time, Water content and Assay values for Formulations F-1 to F-9

Formula	Disintegration time (sec)	Dispersion time (sec)	Water content (w/w)	Assay (%)
F-1	36	71	3.5	99.8
F-2	40	63	3.1	98.3
F-3	62	118	4.2	101.0
F-4	58	109	3.6	99.5
F-5	67	125	4.3	100.7
F-6	49	92	4.0	98.1
F-7	32	65	3.7	99.7
F-8	35	67	3.4	100.2
F-9	34	62	3.5	99.98

Table No. 4: Dissolution Profiles of Different Formulations (F-1 to F-9)

	Cumulative Percentage Drug Release								
Sampling Time (min)	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
10	72.5	50.7	49.6	54.9	56.8	69.6	78.4	77.2	78.0
20	78.0	66.4	63.3	70.0	60.2	80.5	84.3	84.8	85.1
30	83.6	78.5	74.1	79.5	65.3	87.7	90.1	91.4	90.6
40	88.8	87.9	86.4	89.3	73.6	91.4	97.2	98.3	97.4

STABILITY DATA

Table 5: Physical and chemical parameters of Deferasirox dispersible tablets (F-9) after 1st and 2nd month at 40 ± 2°C / 75 ± 5% RH (Packing: HDPE Bottle)

Parameter / Description	Initial	1 month	2 month
	Colour / ShapeLight orange coloured round shaped uncoated tablets	No chang	No change
Avg. wt (mg)	903.0	903.2	903.4
Hardness (kp)	5.89	5.83	5.77
Thickness (mm)	4.41	4.48	4.53
Friability (%)	0.20	0.23	0.26
Water content (w/w)	3.7	3.7	3.7
Assay (%)	99.98	100.5	99.47

SUMMARY AND CONCLUSION

The topic for the present study is "Formulation Development and Evaluation of Deferasirox dispersible tablets".

Introduction is presented in chapter 1 which gives details about chronic iron overload and its mode and choice of drugs for the treatment of chronic iron overload. This chapter also gives the overall view about dispersible tablets and their methods of development.

Materials and methods which gives details about the list of chemicals, equipment used for the study. This chapter also gives information about the methods involved in the development of formulation.

Experimental investigation which gives information about different formulas developed in the formulation of dispersible tablets and the comparative evaluation of the developed formulation with that of the innovator product.Results and discussion which deals with the completed information regarding physical and chemical analysis of the present study with suitable tables, graphs and figures.Deferasirox is indicated in for the treatment of chronic Iron overload due to blood transfusions in adult and pediatric patients (aged 2 years and over). Pre-formulation studies were performed for the drug and excipients as per the standard procedures.

The innovator product characterization was performed.

Formulation 1 was made by direct compression method. In this poor flow property was observed and also hardness and friability values were not satisfactory.

Formulations 2, 3, 4, 6, 7, 8, 9 were made by using wet granulation method. In formulation 2 hardness was found to be less and the friability value does not comply with the specifications. In formulations 3, 4, 6 in order to get a better dispersion the concentration of superdisintegrant was increased. Here the disintegration time, dispersion time and percentage of drug release does not comply with the innovator product. In formulations 7, 8, 9, the disintegration time, dispersion time and percentage of drug release were found to match with the innovator product. All the physicochemical characteristics of the finished product were found to be satisfactory.Formulation 5 was also made by wet granulation method with a different formula. Here the disintegration time, dispersion time and percentage drug release does not match with the innovator.

All the formulations were subjected to physicochemical analysis and out of them Formulation 8 was found to be satisfactory when compared to other formulations. The disintegration time (35 sec), dispersion time (67 sec) and percentage of drug release (98.3%) were found to be satisfactory and it matches with the innovator. So, the batch size was increased in further trial to check the reproducibility (Formulation 9). Finally loaded for stability as per the ICH guidelines.

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