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RESEARCH ARTICLE

Indirect Method for Determination Desferal in Pure and Pharmaceutical Formulations Using Cerium (IV) As a Chelating Element

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Abstract

Objective: The present study includes indirect analytical method for the determination of the drug desferal (DSFM) in some pharmaceutical dosages using molecular absorption. DSFM was usually used for treating such diseases like Thalasemia and Alzheimer. Methods: The proposed method is built on reaction between DSFM and cerium (IV) ion to forms an orange chelate complex (λ max = 443 nm) at pH 6. Results: The optimal experimental condition for the chelate formation: pH=6; concentration of Ce(IV) (30 mg L^{-1}); maximum reaction time (10 min.); λ_{max}=443 nm; metal -to- ligand (1:1) ratio. Analytical figures of merits: linear dynamic range (1-110) mg L^{-1}; r = 0.9996, S = 0.9996 μg.cm^{-2}), D.L (0.167) mg L^{-1}; Erel. % 1.26; recovery% 100.2; RSD% 1.460.Conclusion: The developed method was successfully applied to the estimate of DSFM in pharmaceutical samples.

Keywords: *Desferal, Spectrophotometric, Cerium sulfate tetrahydrate, Pharmaceutical dosages.*

Introduction

Desferrioxamine mesylate (DSFM, Fig. 1), N^1-(5-aminopentyl)-N^1-hydroxy-N^4-(5-(N-hydroxy-4-((5-(N hydroxyacetamido)pentyl) amino)-4-oxobutanamido) pentyl) succinamide methanesulfonate [1]. DSFM is a complex agent with the three-valence iron and aluminum ions and the stability constant of complexes with these elements are shown as 10^{31} and 10^{25} respectively. The chelating occurs on a molecular basis (1: 1) so that theoretically one gram of DSFM can be associated with 85 mg of trivalent iron and 41 mg of trivalent aluminum. DSFM affinity for two-valence ions such as Ca, Zn, Cu and Fe is significantly lower [2]. DSFM is a white powder that dissolves in water and is slightly soluble in methanol and practically does not dissolve in ether and its melting point is 149-148 C^O [3, 4].

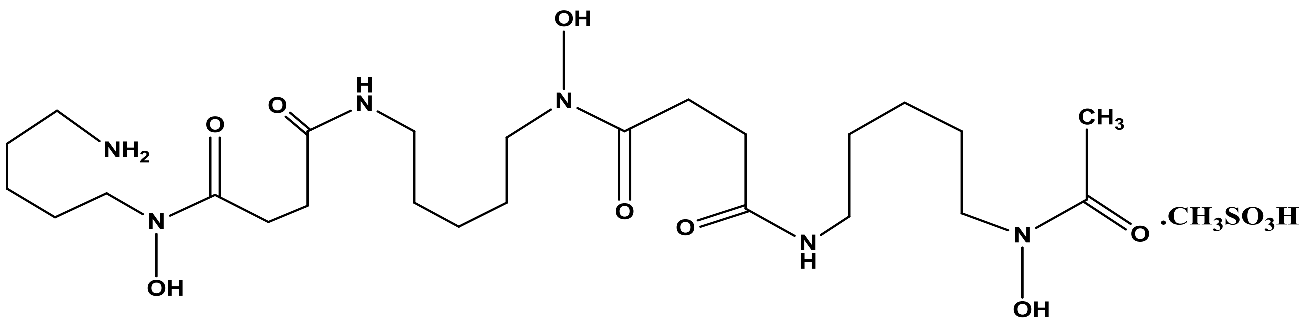

Fig. 1: The chemical structure of desferrioxamine mesylat

The medicine is used in various fields that can be clarified and summarized as follows: It is used to treat Thalassemia [5], it is used to treat increased aluminum burden in patients with kidney failure and bone biopsy [6] and it is used for the treatment of Alzheimer's Disease [7].

The optimization is an analytical method that is performed by studying several factors influencing the analysis. These factors are often chosen from deep knowledge in an analytical way. For example, to develop a spectral method that elects the pH and concentration of the detector as influencing factors in the method.

Factors and the complexity of these factors complicate studies and make them difficult and difficult analytical methods and cannot control all the factors where the purity of the detector cannot be controlled for example, the study of all factors with intensive experiments is very difficult for this study focuses on the factors of counting only prove other factors as much as possible [8].

Rasheed and coworkers [9, 10, 11] investigated the preparation of new chelate complexes (Desferrioxamine mesylate with vanadium and gold ions) and using it for the indirect ET-AAS and molecular absorption for determination DSFM. Recently, Rasheed and coworkers [12, 13] selected a set of ZIC-HILIC column to separate desferrioxamine mesylate as a complex with Al^{+3}, Fe^{+3} and Ce^{+4} ions using ICP-OES as a detection. The objective of work introduced a simple method to determine DSFM in pharmaceutical dosages.

Materials and Methods

All spectral and absorbance measurements were carried out on an Analytik Jena AG-SPECORD 40 UV/Vis Spectrophotometers. Cerium sulfate tetrahydrate and DSFM salt were purchased from Sigma.

Methods

The Optimum Conditions for Determination DSFM

The optimal conditions were studied and controlled, namely the concentration of Ce (IV), pH, reaction time, and the conditions were adjusted for the construction of calibration curves to estimate the DSFM.

Direct Calibration Method

It was transferred volumes between (0.017-1.83) mL of DSFM a concentration of 300 mgL^{-1} to the volumetric flasks capacity 5 mL and then added to each of them (1.5 ml) of the standard solution for Ce (IV) a concentration of 100 mgL^{-1} and the optimal conditions were then adjusted. The volume was diluted to 5 mL with water; the absorbances were measured and plot the calibration curve of the absorbance versus DSFM concentration

Preparation of Desferal Vials

Ten vials of the desferal dosages (500 and 2000 mg of DSFM) were mixed. The 100 mg of mixture was taken and dissolved and diluted with water in a 100 mL volumetric flask.

Result and Discussion

Absorption Spectra

Desferrioxamine Mesylate

Fig. 2 shows the absorption spectra of DSFM. The maximum absorption was at 215 nm of DSFM.

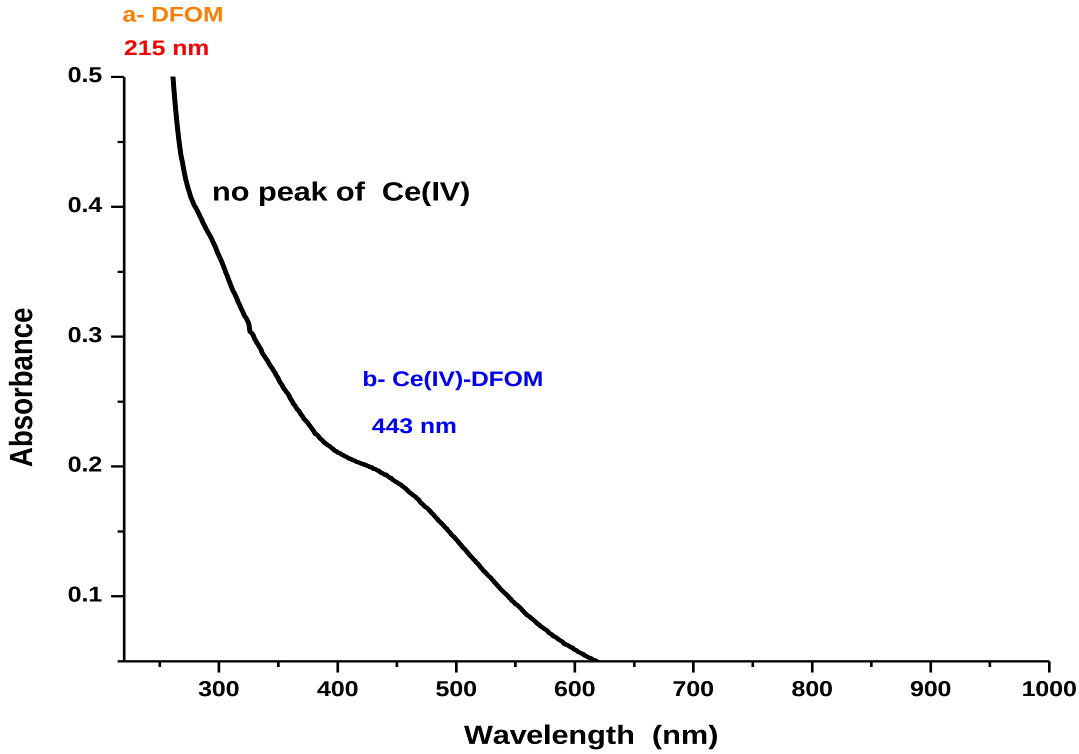

Fig. 2: Absorption spectrum (a) DSFM-100 mg L^{-1} (b) Cerium (IV)-DSFM complex

Cerium (IV) Sulfate Tetrahydrate

The Fig. 3 shows the cerium (IV) spectrum, which shows peak absorption at 274 nm.

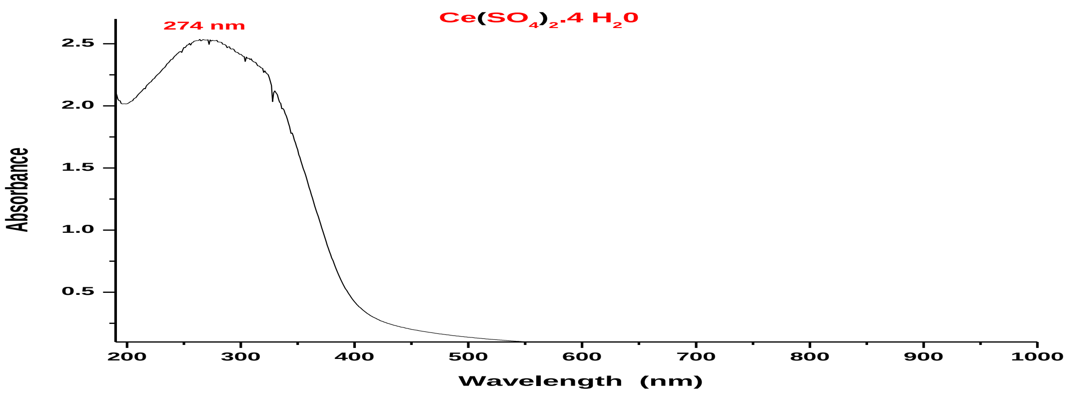

Fig. 3: Absorption spectrum Cerium (IV) sulfates tetrahydrate 20 mg L^{-1}

Complex of DSFM with Cerium (IV)

The absorption spectrum of orange complex (100 mg L^{-1} DSFM-20 mg L^{-1} Ce (IV)) in pH= 6 was 443 nm Fig. 2b.

The Molar Ratio of Ligand (L) to Metal (M)

The molar-ratio method was used to determine the stoichiometry of the complex. A 1: 1 stoichiometric ratio of complex was found as shown in Fig. 4.

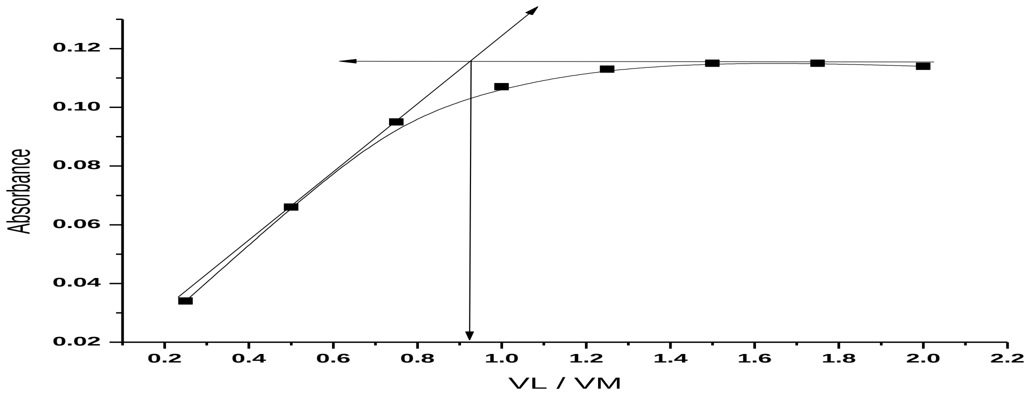

Fig. 4: The stoichiometry of Cerium (IV)-DSFM complex

Optimization of the Method

Influence of Cerium (IV) concentration

Fig. 5 shows the effect of cerium concentration on the complex intestines resulting from DSFM interaction with Ce (IV). The best concentration of the ion that yields the highest absorbance is 30 mg L^{-1}.

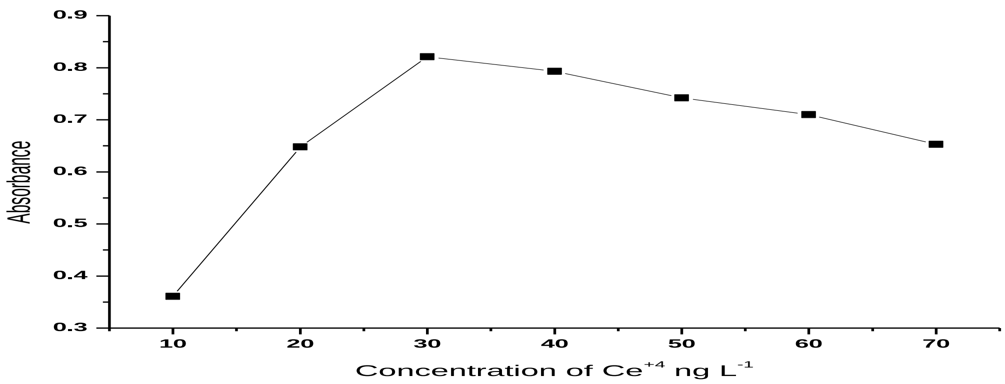

Fig. 5: The effect of Cerium (IV) concentration

Influence of PH

Fig. 6 shows the maximum values of the Cerium (IV)-DSFM complex to pH. The best pH value is 6, with the highest value recorded.

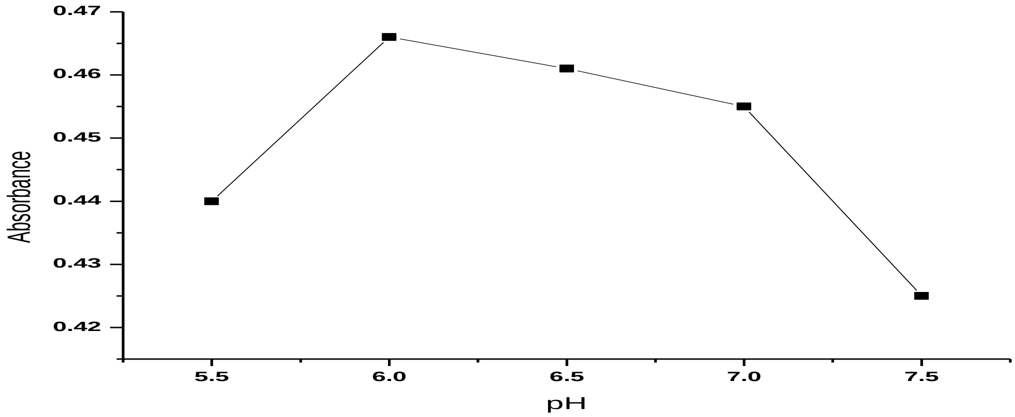

Fig. 6: The effect of pH

Influence of Reaction Time

Fig. 7 indicates that ten minutes are sufficient to complete the complex configuration.

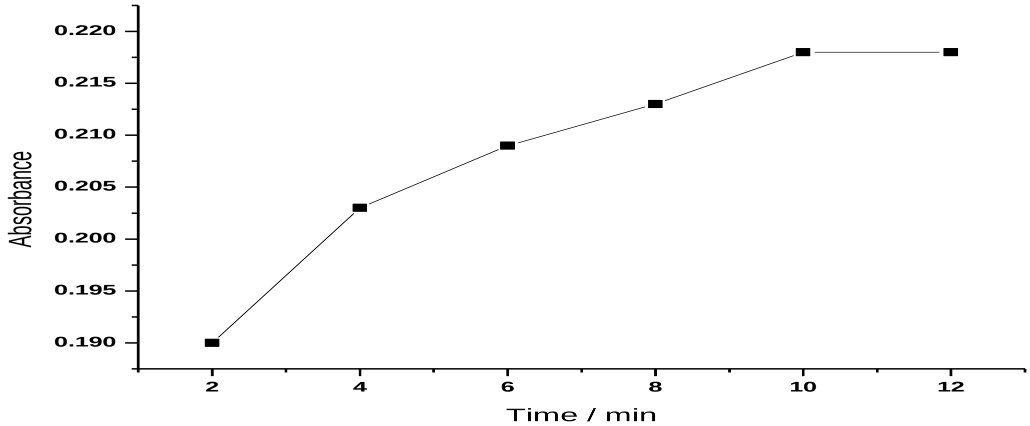

Fig. 7: The Effect of Reaction Time

Calibration Curve for Determination DSFM

Using optimal conditions specified, Fig. 8 shows the direct calibration curve for the DSFM as a Cerium (IV)-DSFM complex, where the maximum concentration of DSFM obeying the Beer's law is up to 110 mg L^{-1}.

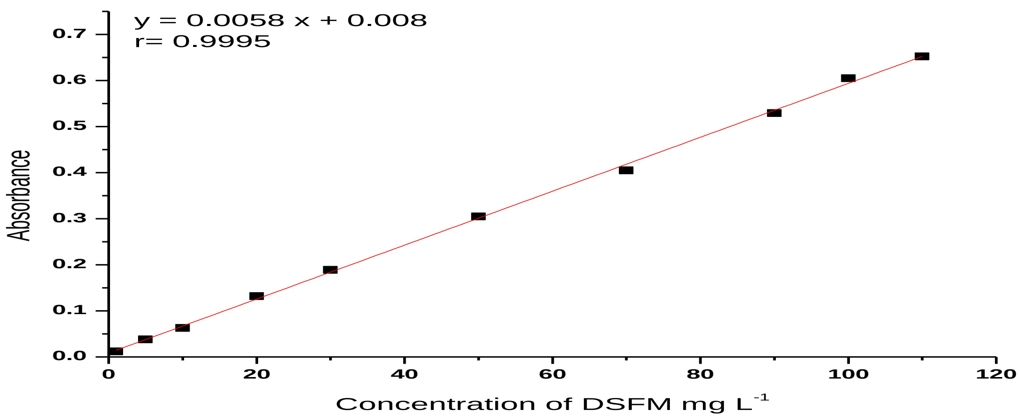

Fig. 8: Calibration curve of DSFM

Method Validation

The calibration graph for the determination of DSFM as a Cerium (IV)-DSFM complex s was constructed and the statistical results are illustrated in Table 1.

Table 1: the statistical results of calibration curve of DSFM

Parameter	Results
Regre. Eq.	y = 0.008 x + 0.0058
Corr. Coef. (r)	0.9996
t- test statistic	59.36
Tabulated t- test two tailed n-2, 95% C.I	2.306
Linearity (mg L^{-1})	1-110
D.L (mg L^{-1}), n=13	0.167
S (µg.cm^{-2})	0.0828
ε (L.mol^{-1} .cm^{-1})	4.29×10^{3}

The accuracy and precision were investigated and calculating by recovery % and RSD %, respectively as shown in Table 2.

Table 2: Precision and accuracy of the indirect method for determination of DSFM as a Cerium (IV)-DSFM complex

Amount of DSFM taken (mg L^{-1})	Amount of DSFM found (mg L^{-1})	Rec. %	Erel. %	RSD % (n=5)
1	1.01	101	1	2.2
50	49.20	98.4	- 1.6	1.7
100	101.23	101.20	1.2	1.6

Determination of DSFM in Pharmaceutical Dosages

The indirect method for determination of DSFM was applied successfully in two of the pharmaceutical dosages; the results summarized in Table 3.

Table 3:

Name of pharmaceutical	Type of dosage	Stated concentration (mg per unit)	Found (mg per unit)	Erel. (%)
Deferoxamine- Novartis Pharma Ltd-Switzerland	Vial	500	490.53	- 1.89
Deferoxamine- Novartis Pharma Ltd-Switzerland	Vial	2000	1988.22	- 0.59

Conclusion

The study, conducted to estimate the drug desferrioxamine mesylate (DSFM) using molecular absorption, showed significant superiority over many other methods in terms of accuracy, sensitivity and speed of analysis.

The study showed the possibility of estimating drugs containing amine groups which can be related to metals and evaluated in molecular absorption method. The analytical results of the molecular spectral method of DSFM showed successfully applied to the determination of DSFM in two pharmaceutical dosages.

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