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Deferiprone, a non-toxic reagent for determination of iron in samples via sequential injection analysis

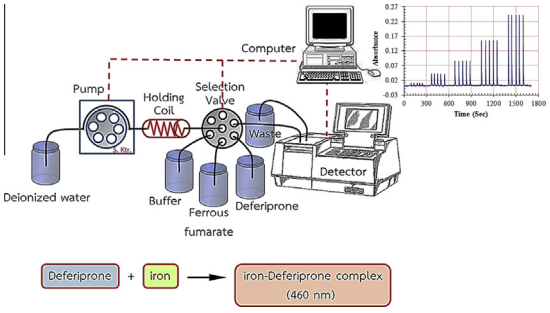
Kraivinee Pragourpun [a], Uthai Sakee [a], Carlos Fernandez [b], Senee Kruanetr [a,*]

[a] Center of Excellence for Innovation in Chemistry and Department of Chemistry (PERCH-CIC), Faculty of Science, Mahasarakham University, Kantarawichai District, Mahasarakham 44150, Thailand
[b] School of Pharmacy and Life Sciences, Robert Gordon University, Aberdeen AB10 7GJ, United Kingdom

HIGHLIGHTS

- We present a green analytical method by using deferiprone as a non-toxic reagent.
- We assemble a simple, rapid, sensitivity and cost effective SIA system for determining iron.
- We use a non-toxic reagent (deferiprone) for determining iron content in real samples in cooperation with the SIA system.

GRAPHICAL ABSTRACT



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ABSTRACT

We present for the first time the use of deferiprone as a non-toxic complexing agent for the determination of iron by sequential injection analysis in pharmaceuticals and food samples. The method was based on the reaction of Fe(III) and deferiprone in phosphate buffer at pH 7.5 to give a Fe(III)–deferiprone complex, which showed a maximum absorption at 460 nm. Under the optimum conditions, the linearity range for iron determination was found over the range of 0.05–3.0 μg mL^{-1} with a correlation coefficient (r^2) of 0.9993. The limit of detection and limit of quantitation were 0.032 μg mL^{-1} and 0.055 μg mL^{-1}, respectively. The relative standard deviation (%RSD) of the method was less than 5.0% (n = 11), and the percentage recovery was found in the range of 96.0–104.0%. The proposed method was satisfactorily applied for the determination of Fe(III) in pharmaceuticals, water and food samples with a sampling rate of 60 h^{-1}.

Introduction

Deferiprone (1,2-dimethyl-3-hydroxy-4-pyridinone) or L1 which is depicted in Fig. 1a is a white crystalline solid with a molecular weight of 139.15 g mol^{-1}. It is an iron chelater indicated for the treatment of patients with transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate. It has a high efficiency for binding iron to form Fe(III)–deferiprone complex with a mole ratio (Fe(III): deferiprone) of 1:3 (Fig. 1b). This complex is stable in an aqueous solution with the maximum absorption wavelength at 450 nm [1–3].

Iron is an essential mineral for health and a component of hemoglobin in the red blood cells which carry oxygen from the lungs to the cells of the body. In addition, it is involved in reactions within the body that produces energy [4]. Iron is generally found in water and food such as liver, beef, pork, tofu, soybean, cereals, spinach, watercress, etc. In pharmaceutical it can be found in the iron form such as ferrous fumarate. A lack of iron affects the

* Corresponding author. Tel.: +66 043 754246x1128; fax: +66 043 754246.
E-mail address: Seiney@yahoo.com (S. Kruanetr).

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development of the red blood cells and causes iron deficiency anemia [5]. In order to avoid such deficiencies, an adequate supply of iron is needed. Ferrous fumarate [6], is a drug formula that provides the body with the extra amounts of iron. It is used to treat or prevent iron deficiency anemia, a condition that occurs when the body has fewer red blood cells than it needs owing to a poor diet, excess bleeding, or as the result of other medical problem.

Sequential injection analysis (SIA) is one of the flow-based analytical techniques that is used for the determination of iron in various samples with emphatic advantages such as simplicity, rapidity, sensitivity, reproducibility, flexibility and low chemical consumption [7]. However, the drawback has emerged because most of the reagents employed such as tiron [8], 1,10 phenantroline [9], 2-(5-bromo-2-pyridylazo)-5-[*N*-*n*-propyl-*N*-(3-sulfopropyl) amino] aniline [10] and ferrozine [11] are toxic and have health impacts on humans. The developing of a non-toxic reagent which is sensitive, less toxic chemical in waste production, cost effective and human friendly is needed. In drug formulations norflocaxin [12] which is a less toxic reagent for iron determination has been used in batch-wise method. Liawrungrath et al. employed Flow Injection analysis along with norflocaxin [13] for the determination of Fe(III). Ruengsitagoon [14] used FIA with chlortetracycline to detect Fe(III). Grudpan et al. [15] also utilized FIA with aspirin to determine the amount of Fe (III) in the solution. Although those methods use drugs which are less toxic, the drawbacks of theses technique are higher amounts of chemical consumption and waste production when compared to the SIA technique. There are some publications which have developed the SIA system using the complexing agent for simultaneous analysis of Fe(II) and Fe(III) in samples such as Viollier et al. [16] modified the SIA system using ferrozine for determining the Fe(II) and Fe(III) speciation in small volumes of fresh and marine water samples. Galhardo et al. [17] applied the SIA using 1,10-phenantroline and reducing agent as a tool for in situ monitoring of Fe(II) and Fe(III) in natural and waste waters. Kass and Ivaska [18] presented the SIA method using tiron for determination of total iron in a pilot plant of a zinc process. Mulaudzi et al. [19] demonstrated the SIA system for speciation of iron by determining Fe(III) with tiron, followed by the determination of total iron which includes the Fe(III) produced from the oxidation of Fe(II) using hydrogen peroxide. Although the presented methods are specific and sensitive, but they are still using a toxic reagent. Therefore, to solve this problem the use of a non-toxic reagent along with the SIA for the determination of iron is an attractive alternative technique.

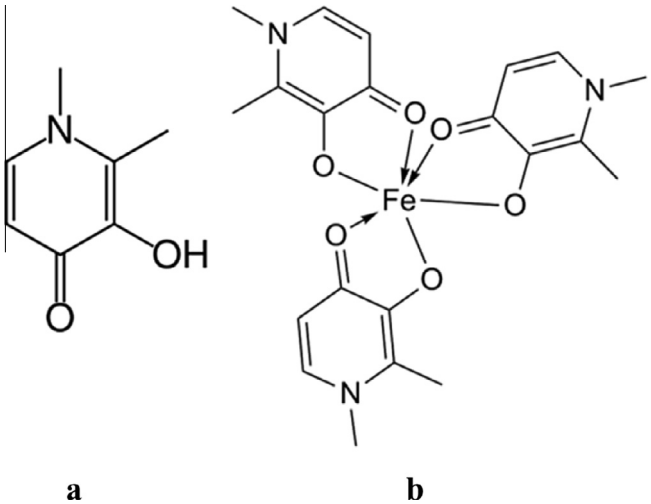

Fig. 1. (a) Chemical structure of deferiprone (b) Fe(III)–deferiprone complex.

In this issue we present the use of deferiprone, a non-toxic complexing reagent for the determination of iron in samples (ferrous fumarate tablets, water sample and food sample) by using the SIA system. The method is based on the measurement of the absorbance of Fe(III)–deferiprone complex which is formed between iron(III) and deferiprone in the buffer solution. The optimum conditions for determining iron content were also investigated.

Experimental

Chemicals

The chemicals used were of analytical reagent grade and employed without any further purification. Deionized water was used for preparation and/or diluted solutions throughout the experiments.

Working stock standard solution of Fe(III) (10.0 μg mL^{-1}) was prepared by diluting 5.00 mL of 1000 μg mL^{-1} stock standard Fe(III) solution (AAS standard, Merck, Germany) into a 500 mL volumetric flask and adjusting the volume with 1.0% nitric acid. Working solutions were prepared by appropriate dilution of the working stock solution.

Buffer solutions ranging from pH 3 to pH 6 and from pH 6 to pH 9 were prepared by mixing an appropriate ratio of 0.1 mol L^{-1} acetic acid with 0.1 mol L^{-1} sodium acetate ($C_2H_3O_2Na$: 8.204 g L^{-1}), and 0.1 mol L^{-1} disodium hydrogen phosphate ($Na_2HPO_4{\cdot}2H_2O$: 11.87 g L^{-1}) with 0.1 mol L^{-1} potassium dihydrogen phosphate (KH_2PO_4: 9.073 g L^{-1}), respectively. The required pH was achieved by adjusting with 1.00 mol L^{-1} sodium hydroxide and/or 1.0%v/v hydrochloric acid.

A 1.0 mmol L^{-1} deferiprone stock solution was prepared by dissolving 0.0070 g of fine powder deferiprone (20 capsules, each capsule containing 500 mg of deferiprone) in deionized water and adjusted to volume in a 50 mL volumetric flask. The working solution of deferiprone was prepared by appropriate dilution of the stock solution with phosphate buffer pH 7.5.

Apparatus

The assembled SIA system used in this work was depicted in Fig. 2. It consisted of a computer controlled peristaltic pump (Reglo digital ISM 834, ISMATEC Co., Inc.) (P) with Tygon pump tubing (1.02 mm i.d. and 2.25 mm o.d.) which was connected to PTFE tubing that was immerged into the deionization water reservoir as a carrier (C). A ten-port selection valve (VICI, Valco Instrument, USA) (SV) controlled by a computer software was used for the aspiration of all solutions into the system. PTFE tubing 1.02 mm i.d. and 150 cm long was used as the holding coil (HC) that was placed between the pump and valve. Deferiprone solution (R), sample or standard Fe(III) solution (S) and phosphate buffer solution pH 7.5 reservoirs (B) were introduced into the system via the selection valve through PTFE tubing. A UV–Vis spectrophotometer (Perkin Elmer lambda 25) with a flow through cell (10 mm path length) was used as the detector (D). A personal computer with special software was used for collection of signals and control of all devices in the system.

Sample preparation

Ferrous fumarate tablets were purchased from drug store and prepared according to the standard USP method [20]. About 0.1 g of the drug powder (20 tablets) was accurately weighed and transferred into a 250 mL beaker containing 25 mL of water, 2.5 mL of nitric acid and 7.5 mL of perchloric acid. The solution was heated and evaporated to a volume of approximately 1 mL. It was then