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Ferrosoferric Oxide

$Fe_3O_4(FeO \cdot Fe_2O_3)$ 231.54
Magnetite;
Ferrous-ferric oxide;
Iron (II, III) oxide CAS RN®: 1317-61-9.

DEFINITION

Ferrosoferric Oxide contains NLT 97.0% and NMT 100.5% of Fe_2O_3, calculated on the ignited basis.

IDENTIFICATION

- **A.**

Sample solution: Dissolve 0.1 g in 5 mL of hydrochloric acid, and dilute with water to 50 mL.

Analysis 1: Transfer 5 mL of the *Sample solution* to a test tube, and add a few drops of potassium ferrocyanide TS.

Analysis 2: Transfer 5 mL of the *Sample solution* to a test tube, and add a few drops of potassium ferricyanide TS.

Acceptance criteria: For both *Analysis 1* and *Analysis 2*, a blue precipitate (Prussian blue) is formed, which does not dissolve in dilute hydrochloric acid subsequently added. The precipitate dissolves in oxalic acid and sodium or potassium hydroxide.

- **B.** Ferrosoferric Oxide presents as black powder, which is distinguished from ferric oxide exhibiting two basic colors (red and yellow). It is attracted to a magnet.

ASSAY

- **PROCEDURE**

To enable the calculation of the percentage of Fe_2O_3 on the ignited basis, ignite about 2 g at 800 ± 25° to constant weight as directed in *Loss on Ignition ⟨733⟩*. [NOTE—Ignited Ferrosoferric Oxide is hygroscopic.]

Sample: 1.5 g

Blank: 25 mL of hydrochloric acid

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Direct titration

Titrant: 0.1 N sodium thiosulfate VS

Endpoint detection: Visual

Analysis: Digest the *Sample* in 25 mL of hydrochloric acid on a water bath until dissolved. Add 10 mL of hydrogen peroxide TS, and evaporate on a water bath almost to dryness in order to volatilize all hydrogen peroxide. Dissolve the residue by warming with 5 mL of hydrochloric acid; add 25 mL of water; filter into a 250-mL volumetric flask, washing the filter with water; and add water to volume. Transfer a 50-mL aliquot to a glass-stoppered flask, add 3 g of potassium iodide and 5 mL of hydrochloric acid, and insert the stopper into the flask. Allow the mixture to stand for 15 min, add 50 mL of water, and titrate the liberated iodine with 0.1 N sodium thiosulfate VS, using starch TS as the indicator. Perform a blank determination in the same manner.

Calculate the percentage of the labeled amount as ferric oxide (Fe_2O_3) in the portion of the *Sample* taken:

$$\text{Result} = \{[(V_S - V_B) \times N \times F]/W\} \times 100$$

V_S = *Titrant* volume consumed by the *Sample* (mL)

V_B = *Titrant* volume consumed by the *Blank* (mL)

N = actual normality of the *Titrant* (mEq/mL)

F = equivalency factor, 79.85 mg/mEq

W = weight of the *Sample*, calculated with a correction for loss on ignition (mg)

Acceptance criteria: 97.0%–100.5% on the ignited basis

IMPURITIES

• **Limit of Arsenic (As)**

[Note—Select all reagents to have as low contents of elemental impurities as practicable, and store all reagent solutions in containers of borosilicate glass. Cleanse all glassware before use by soaking in warm 8 N nitric acid for 30 min and by rinsing with deionized water.]

Solvent: 10% hydrochloric acid in water

Standard stock solution: Prepare a solution containing 2 ppm of arsenic from an Arsenic ICP/AA standard solution in *Solvent*. [Note—A commercially available certified standard solution can be used.]

Sample stock solution: In a 100-mL volumetric flask, dissolve 5.0 g of Ferrosoferric Oxide in 50 mL of hydrochloric acid by heating without boiling for about 1 h until the sample is dissolved. Cool down to room temperature. Pass through a filter, if necessary. Dilute with water to volume. Transfer 20.0 mL of the solution to a 100-mL volumetric flask, add 40 mL of ascorbic acid solution (200 mg/mL of ascorbic acid in water) and 20 mL of potassium iodide solution (400 mg/mL of potassium iodide in water), and dilute with water to volume. [Note—Reduce arsenic to the lowest possible oxidation state.] The resulting solution contains 10 mg/mL (g/L) of Ferrosoferric Oxide.

Sample solution A: Transfer 20 mL of the *Sample stock solution* to a 100-mL volumetric flask. Dilute with *Solvent* to volume. The resulting solution contains 2 mg/mL (g/L) of Ferrosoferric Oxide.

Sample solution B: Transfer 20 mL of the *Sample stock solution* to a 100-mL volumetric flask. Add 25 mL of the *Standard stock solution*, and dilute with *Solvent* to volume.

Sample solution C: Transfer 20 mL of the *Sample stock solution* to a 100-mL volumetric flask. Add 50 mL of the *Standard stock solution*, and dilute with *Solvent* to volume.

Blank: *Solvent*

Instrumental conditions

(See *Atomic Absorption Spectroscopy ⟨852⟩*.)

Mode: Atomic absorption spectrophotometer

Lamp: Arsenic hollow-cathode

Flame: Air–acetylene

Analytical wavelength: 193.696 nm

Analysis

Samples: *Sample solution A*, *Sample solution B*, and *Sample solution C*

[Note—To minimize matrix interference, it is recommended that the method of standard additions be used.]

Determine the absorbances of the *Samples* against the *Blank*, and plot the corrected absorbances versus their added content of arsenic (0, 0.5, and 1.0 ppm). Draw the straight line best fitting the three points, and extrapolate the line until it meets the concentration axis. The distance between this point and the intersection of the axes represents the concentration of arsenic, C_A, in ppm (µg/g) in the 2 mg/mL of Ferrosoferric Oxide in *Solvent*.

Calculate the content of arsenic, in µg/g, in the portion of Ferrosoferric Oxide taken:

$$\text{Result} = C_A \times D$$

D = dilution factor, 25

Acceptance criteria: NMT 2 ppm

• **Limit of Cadmium (Cd) and Chromium (Cr)**

[Note—Select all reagents to have as low contents of elemental impurities as practicable, and store all reagent solutions in containers of borosilicate glass. Cleanse all glassware before use by soaking in warm 8 N nitric acid for 30 min and by rinsing with deionized water.]

Solvent: 10% hydrochloric acid in water

Standard stock solution: Prepare a solution containing 2 ppm each of cadmium and chromium from an ICP standard solution containing cadmium and chromium in *Solvent*. [Note—A commercially available certified standard solution can be used.]

Sample stock solution: In a 100-mL volumetric flask, dissolve 5.0 g of Ferrosoferric Oxide in 50 mL of hydrochloric acid by heating without boiling for about 1 h until the sample is dissolved. Cool down to room temperature. Pass through a filter, if necessary. Dilute with water to volume. Transfer 20.0 mL of the solution to a 100-mL volumetric flask, and add water to volume. The resulting solution contains 10 mg/mL of Ferrosoferric Oxide.

Sample solution A: Transfer 20 mL of the *Sample stock solution* to a 100-mL volumetric flask. Dilute with *Solvent* to volume. The resulting solution contains 2 mg/mL of Ferrosoferric Oxide.

Sample solution B: Transfer 20 mL of the *Sample stock solution* to a 100-mL volumetric flask. Add 25 mL of the *Standard stock solution*, and dilute with *Solvent* to volume.

Sample solution C: Transfer 20 mL of the *Sample stock solution* to a 100-mL volumetric flask. Add 50 mL of the *Standard stock solution*, and dilute with *Solvent* to volume.

Blank: *Solvent*

Instrumental conditions

(See Plasma Spectrochemistry ⟨730⟩.)

Mode: Inductively coupled plasma–atomic emission spectrometer (ICP–AES)

Analytical wavelength

Cadmium: 228.802 nm

Chromium: 267.716 nm

Analysis

Samples: *Sample solution A*, *Sample solution B*, and *Sample solution C*

[NOTE—The operating conditions may be developed and optimized based on the manufacturer's recommendation.]

[NOTE—To minimize matrix interference, it is recommended that the method of standard additions be used.]

Instrument performance must be verified to conform to the manufacturer's specifications for resolution and sensitivity. Before analyzing samples, the instrument must pass a suitable performance check. Aspirate the *Samples*, at least in duplicate, and calculate the average absorbances for each against the *Blank*. Plot the average absorbances of the *Samples* versus their added content (0, 0.5, and 1.0 ppm) of cadmium (or chromium). Draw the straight line best fitting the three points, and extrapolate the line until it intercepts the concentration axis. The distance between this point and the intersection of the axes represents the concentration of cadmium (or chromium), C_C, in ppm (µg/g) in the 2 mg/mL of Ferrosoferric Oxide in *Solvent*.

Calculate the content of cadmium (or chromium), in µg/g, in the portion of Ferrosoferric Oxide taken:

$$\text{Result} = C_C \times D$$

D = dilution factor, 25

Acceptance criteria

Cadmium: NMT 1 ppm

Chromium: NMT 100 ppm

- **LIMIT OF LEAD (PB)**

[NOTE—Select all reagents to have as low contents of elemental impurities as practicable, and store all reagent solutions in containers of borosilicate glass. Cleanse all glassware before use by soaking in warm 8 N nitric acid for 30 min and by rinsing with deionized water.]

Solvent: 4% hydrochloric acid and 8% nitric acid in water

Standard solution: Prepare a solution containing 25 ppb of lead in *Solvent*. [NOTE—A commercially available certified standard solution can be used.]

Sample stock solution: Dissolve 1.0 g of Ferrosoferric Oxide in 4 mL of hydrochloric acid and 8 mL of nitric acid in a 100-mL volumetric flask by heating without boiling until the sample is dissolved. Cool down to room temperature. Pass through a filter, if necessary. Dilute with water to volume. The resulting solution in the flask contains 10 mg/mL of Ferrosoferric Oxide.

Sample solution A: Transfer 10 mL of the *Sample stock solution* to a 100-mL volumetric flask, and dilute with *Solvent* to volume. The solution contains 1 mg/mL of Ferrosoferric Oxide.

Sample solution B: Transfer 10 mL of the *Sample stock solution* to a 100-mL volumetric flask. Add 4 mL of the *Standard solution*, and dilute with *Solvent* to volume.

Sample solution C: Transfer 10 mL of the *Sample stock solution* to a 100-mL volumetric flask. Add 12 mL of the *Standard solution*, and dilute with *Solvent* to volume.

Sample solution D: Transfer 10 mL of the *Sample stock solution* to a 100-mL volumetric flask. Add 20 mL of the *Standard solution*, and dilute with *Solvent* to volume.

Blank: *Solvent*

Instrumental conditions

(See Atomic Absorption Spectroscopy ⟨852⟩.)

Mode: Atomic absorption spectrophotometer equipped with graphite heating device

Analytical wavelength: 283.3 nm

Lamp: Lead hollow-cathode

Analysis

Samples: *Sample solution A*, *Sample solution B*, *Sample solution C*, and *Sample solution D*

[NOTE—To minimize matrix interference, it is recommended that the method of standard additions be used.]

Determine the absorbances of the *Samples* against the *Blank*, and plot the corrected absorbances versus their added content (0, 1, 3, and 5 ppb) of lead. Draw the straight line best fitting the four points, and extrapolate the line until it intercepts the concentration axis. The distance between this point and the intersection of the axes represents the concentration of lead, C_L, in ppm (µg/g) in the 1 mg/mL of Ferrosoferric Oxide.

Calculate the content of lead, in µg/g, in the portion of Ferrosoferric Oxide taken:

$$\text{Result} = C_L \times D$$

D = dilution factor, 10

Acceptance criteria: NMT 10 ppm

- **LIMIT OF MERCURY (HG) AND NICKEL (NI)**

[NOTE—Select all reagents to have as low contents of elemental impurities as practicable, and store all reagent solutions in containers of borosilicate glass. Cleanse all glassware before use by soaking in warm 8 N nitric acid for 30 min and by rinsing with deionized water.]

Solvent: 10% hydrochloric acid in water

Standard solution: Prepare a solution containing 2 ppm of mercury (or nickel) from a Mercury (or Nickel) ICP/AA standard solution in *Solvent*. [NOTE—A commercially available certified standard solution can be used.]

Sample stock solution: In a 100-mL volumetric flask, dissolve 5.0 g of Ferrosoferric Oxide in 50 mL of hydrochloric acid by heating without boiling for about 1 h until the sample is dissolved. Cool down to room temperature. Pass through a filter, if necessary. Dilute with water to volume. Transfer 20.0 mL of the solution to a 100-mL volumetric flask, and add water to volume. The resulting solution contains 10 mg/mL of Ferrosoferric Oxide.

Sample solution A: Transfer 20 mL of the *Sample stock solution* to a 100-mL volumetric flask. Dilute with *Solvent* to volume. The resulting solution contains 2 mg/mL of Ferrosoferric Oxide.

Sample solution B: Transfer 20 mL of the *Sample stock solution* to a 100-mL volumetric flask. Add 25 mL of the *Standard solution*, and dilute with *Solvent* to volume.

Sample solution C: Transfer 20 mL of the *Sample stock solution* to a 100-mL volumetric flask. Add 50 mL of the *Standard solution*, and dilute with *Solvent* to volume.

Blank: *Solvent*

Instrumental conditions

(See *Atomic Absorption Spectroscopy 〈852〉*.)

Mode: Atomic absorption spectrophotometer

Detection

Mercury: Flameless

Nickel: Air–acetylene flame

Lamp: Mercury hollow-cathode or nickel hollow-cathode

Analytical wavelength

Mercury: 253.7 nm

Nickel: 231.604 nm

Analysis

Samples: *Sample solution A*, *Sample solution B*, and *Sample solution C*

[NOTE—To minimize matrix interference, it is recommended that the method of standard additions be used.]

Determine the absorbances of the *Samples* against the *Blank*, and plot the corrected absorbances versus their content (0, 0.5, and 1.0 ppm) of mercury (or nickel). Draw the straight line best fitting the three points, and extrapolate the line until it intercepts the concentration axis. The distance between this point and the intersection of the axes represents the concentration of mercury (or nickel), C_S, in ppm (µg/g) in the 2 mg/mL of Ferrosoferric Oxide in *Solvent*.

Calculate the content of mercury (or nickel), in µg/g, in the portion of Ferrosoferric Oxide taken:

$$\text{Result} = C_S \times D$$

D = dilution factor, 25

Acceptance criteria

Mercury: NMT 1 ppm

Nickel: NMT 200 ppm

SPECIFIC TESTS

- **WATER-SOLUBLE SUBSTANCES**

Sample: 2.0 g

Analysis: Digest the *Sample* in 100 mL of water on a boiling water bath for 2 h, filter, and wash the filter with water. Evaporate the filtrate and washings, and dry the residue at 105° for 1 h.

Acceptance criteria: The weight of the dried residue is NMT 20 mg, corresponding to NMT 1.0%.

- **Acid-Insoluble Substances**

Sample: 2.0 g

Analysis: Digest the *Sample* in 25 mL of hydrochloric acid by boiling for 20 min. Add 100 mL of hot water, and filter quantitatively through a tared filtering[1] crucible, with the aid of hot wash water, until the filtrate tests negative for chloride. Dry the crucible and contents at 105° for 1 h.

Acceptance criteria: The weight of the residue is NMT 6 mg, corresponding to NMT 0.3%.

- **Organic Colors and Lakes**

Analysis: Place 1.0 g in each of 3 beakers, and add 25 mL of each of the following reagents, respectively: 1-chloronaphthalene, alcohol, and chloroform. Heat the beakers containing alcohol and chloroform just to boiling. Heat the other beaker on a boiling water bath for 15 min, with occasional swirling. Pass the contents of the beakers through retentive, solvent-resistant filter paper.[2] If any of the filtrates show visible turbidity, centrifuge for 15 min. Record the spectra against respective solvent blanks in 1-cm cells from 350 to 750 nm.

Acceptance criteria: Absorbance in the range of 350–750 nm is NMT 0.01 AU.

- **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^3 cfu/g, and the total combined molds and yeasts count does not exceed 10^2 cfu/g.
- **pH ⟨791⟩:** 6–9 in a 10% suspension
- **Loss on Drying ⟨731⟩**

Analysis: Dry a sample at 105° for 1 h.

Acceptance criteria: NMT 1.0% of its weight

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature.

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[1] A glass-filter disc (P4; pore size diameter 9 to 15 µm) can be used, or equivalent.

[2] A PTFE filter (diameter 25 mm, 0.2-µm pore size), or equivalent.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
FERROSOFERRIC OXIDE	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

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