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Iron Sucrose Injection

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DEFINITION

Iron Sucrose Injection is a sterile, colloidal solution of ferric hydroxide in complex with Sucrose in Water for Injection. It contains NLT 95.0% and NMT 105.0% of the labeled amount of iron. Sodium Hydroxide may be added to adjust the pH. It contains no antimicrobial agent, chelating agent, dextran, gluconate, or other added substances.

IDENTIFICATION

• A. IRON

To 2.5 mL of Injection add 17.5 mL of [water](#) and 5 mL of [hydrochloric acid](#). Mix and heat the solution for 5 min in a boiling water bath. Cool, add dropwise 13.5 N [ammonium hydroxide](#) until no further precipitation of ferric hydroxide occurs, and filter. Wash the precipitate with [water](#) to remove excess ammonium hydroxide, dissolve the precipitate in a minimum volume of 2 N [hydrochloric acid](#), and add sufficient [water](#) to make a volume of 20 mL. To 3 mL of the solution add 1 mL of 2 N [hydrochloric acid](#) and 1 mL of [potassium thiocyanate TS](#): the resulting solution (Solution 1) is red. To 1 mL of Solution 1 add 5 mL of [amyl alcohol](#) or [ethyl ether](#), shake, and allow to stand: the organic layer is pink. To a separate 1-mL aliquot of Solution 1 add 2 mL of [mercuric chloride TS](#): a red color is discharged [iron (III) salts].

• B. The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay for Sucrose.

• C. MOLECULAR WEIGHT DETERMINATION

Mobile phase: Dissolve 7.12 g of [sodium phosphate, dibasic, dihydrate](#), 5.52 g of [sodium phosphate, monobasic](#) and 0.40 g of [sodium azide](#) in 2 L of [water](#).

System suitability solution: Dissolve 200 mg of [high molecular weight dextran](#) and 100 mg of [glucose](#) in 20 mL of *Mobile phase*.

Standard solutions: Transfer about 20 mg of each [polysaccharide molecular weight standard](#) (5,000–400,000 Da) to separate 5-mL volumetric flasks. Add 4 mL of *Mobile phase* to each flask, and allow each aliquot to stand at or below 25° for a minimum of 12 h. After the agglomerate particles of each *Standard solution* have swelled to their fullest extent, gently swirl each *Standard solution* until dissolved. [NOTE—The chromatograms of freshly prepared *Standard solutions* regularly show a small, unidentified secondary peak following the main peak. Discard the *Standard solutions* if the secondary peak reaches half the height of the main peak.]

Sample solution: Transfer 5.0 mL of Injection to a 10-mL volumetric flask, and dilute with *Mobile phase* to volume.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: Refractive index, maintained at a constant temperature of 45°

Columns: Two 7.8-mm × 30-cm; packing [L39](#) with pore sizes of 1000 and 120 Å, respectively

Column temperature: 45 ± 2°

Flow rate: 0.5 mL/min

Injection volume: 25 µL

System suitability

Samples: *System suitability solution* and *Standard solutions*

Suitability requirements

Resolution: NLT 4.0 between dextran and glucose, *System suitability solution*

Correlation coefficient: NLT 0.98 for the calibration curve generated using a suitable program, plotting the retention times of the *Standard solutions* and their molecular weights to generate a third order (cubic) calibration curve

Analysis

Samples: *System suitability solution*, *Standard solutions*, and *Sample solution*

The molecular weight of the complex is calculated from the calibration curve. The molecular weight distribution curve of the sample is sliced into fractions.

Calculate the weight-average molecular weight (M_w) as follows:

$$\text{Result} = \Sigma(A_i M_i) / \Sigma A_i$$

Calculate the number-average molecular weight (M_n) as follows:

$$\text{Result} = \Sigma(A_T) / \Sigma(A_T/M_T)$$

A_T = area of each fraction of the sample distribution

M_T = corresponding mean molecular weight of each fraction as determined from its retention time on the calibration curve

Acceptance criteria: The molecular weight distribution curve of the Injection conforms to the following parameters.

M_w : 34,000–60,000 Da

M_n : NLT 24,000 Da

M_w/M_n : NMT 1.7

ASSAY

• SUCROSE

Mobile phase: [Acetonitrile](#) and [water](#) (79:21)

Standard solutions: Individual solutions of 13, 16, 18, 21, and 23 mg/mL of sucrose from [USP Sucrose RS](#), in [water](#)

Sample solution: Transfer about 1.875 g of Injection to a 25-mL flask. Add 1.25 mL of [water](#) and mix. Add 1.25 mL of a [sodium phosphate, monobasic](#) solution, prepared by dissolving 30 g in 50 mL, and mix. Allow the resulting solution to stand for 10 min to precipitate the colloidal ferric hydroxide. Dilute with [water](#) to volume. Centrifuge this solution at 3000 rpm for 15 min. Pass the resulting solution through a filter, discarding the first 2 mL of the filtrate.

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: Refractive index

Column: 4-mm × 25-cm; packing [L8](#)

Temperatures

Detector: 20–25° (±2°)

Column: 20–25° (±2°)

Flow rate: 2 mL/min

Injection volume: 20 µL

System suitability

Samples: *Standard solutions*

[NOTE—The retention time for sucrose is about 8 min.]

Suitability requirements

Correlation coefficient: NLT 0.998 from the linear regression of the *Standard solutions*

Analysis

Samples: *Standard solutions* and *Sample solution*

Plot the peak area for each *Standard solution* versus concentration of sucrose in mg/mL, and draw the straight line best fitting the five plotted points. From the graph, determine the concentration of sucrose, in mg/mL, in the *Sample solution*.

Calculate the quantity of sucrose, in mg, in each mL of Injection taken:

$$\text{Result} = (C_U \times D \times G) / W$$

C_U = concentration of sucrose in the *Sample solution* (mg/mL)

D = dilution volume of the *Sample solution* (mL)

G = density of Injection taken (g/mL)

W = weight of Injection taken (g)

Acceptance criteria: 260–340 mg/mL

• IRON

Solution A: Transfer 2.64 g of [calcium chloride](#) to a 1000-mL volumetric flask, add 500 mL of [water](#), and swirl to dissolve. Add 5.0 mL of [hydrochloric acid](#), and dilute with [water](#) to volume.

Standard stock solution: 50 µg/mL of iron prepared as follows. Transfer about 350 mg of [ferrous ammonium sulfate](#) to a 1000-mL volumetric flask. Add [water](#) to dissolve, dilute with [water](#) to volume, and mix.

Standard solutions: Individual solutions containing 2.0, 4.0, 6.0, 8.0, and 10.0 µg/mL of iron in *Solution A* from the *Standard stock solution*

Sample stock solution: Using a “to contain” pipet, transfer 2.0 mL of Injection to a 100-mL volumetric flask. Rinse the pipet several times with *Solution A*. Add 5 mL of [hydrochloric acid](#), and swirl until the solution turns yellow. After the solution has cooled to room temperature, dilute with *Solution A* to volume, and mix.

Sample solution: Nominally 8.0 µg/mL of iron prepared as follows. Pipet 2.0 mL of the *Sample stock solution* to a 100-mL volumetric flask, and dilute with *Solution A* to volume.

Instrumental conditions

(See [Atomic Absorption Spectroscopy \(852\)](#).)