Heavy metals (*2.4.8*): maximum 50 ppm.

Dissolve 1.0 g in 10 mL of *hydrochloric acid R1*. Add 2 mL of *strong hydrogen peroxide solution R*, then evaporate to 5 mL. Allow to cool and dilute to 20 mL with *hydrochloric acid R1* and transfer the solution to a separating funnel. Shake 3 times, for 3 min each time, with 20 mL of *methyl isobutyl ketone R1*. Separate the lower phase, reduce to half its volume by evaporation and dilute to 25 mL with *water R*. Neutralise 10 mL of the solution with *dilute ammonia R1* to *red litmus paper R* and dilute to 20 mL with *water R*. 12 mL of the solution complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

ASSAY

In a conical flask with a ground-glass stopper, dissolve 0.200 g in 20 mL of *water R*. Add 10 mL of *dilute hydrochloric acid R* and 2 g of *potassium iodide R*. Allow the stoppered flask to stand for 1 h protected from light. Titrate with *0.1 M sodium thiosulfate*, adding 5 mL of *starch solution R* towards the end of the titration.

1 mL of *0.1 M sodium thiosulfate* is equivalent to 27.03 mg of $FeCl_3,6H_2O$.

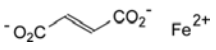
STORAGE

In an airtight container, protected from light.

01/2008:0902
corrected 7.0

FERROUS FUMARATE

Ferrosi fumaras



$C_4H_2FeO_4$ M_r 169.9
[141-01-5]

DEFINITION

Iron(II) (*E*)-butenedioate.

Content: 93.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: fine, reddish-orange or reddish-brown powder.

Solubility: slightly soluble in water, very slightly soluble in ethanol (96 per cent).

IDENTIFICATION

A. Thin-layer chromatography (*2.2.27*).

Test solution. To 1.0 g add 25 mL of a mixture of equal volumes of *hydrochloric acid R* and *water R* and heat on a water-bath for 15 min. Cool and filter. Use the filtrate for identification test C. Wash the residue with 50 mL of a mixture of 1 volume of *dilute hydrochloric acid R* and 9 volumes of *water R* and discard the washings. Dry the residue at 100-105 °C. Dissolve 20 mg of the residue in *acetone R* and dilute to 10 mL with the same solvent.

Reference solution. Dissolve 20 mg of *fumaric acid CRS* in *acetone R* and dilute to 10 mL with the same solvent.

Plate: *TLC silica gel F_{254} plate R*.

Mobile phase: *anhydrous formic acid R, methylene chloride R, butanol R, heptane R* (12:16:32:44 *V/V/V/V*).

Application: 5 µL.

Development: in an unsaturated tank, over a path of 10 cm.

Drying: at 105 °C for 15 min.

Detection: examine in ultraviolet light at 254 nm.

Results: the principal spot in the chromatogram obtained with the test solution is similar in position and size to the principal spot in the chromatogram obtained with the reference solution.

B. Mix 0.5 g with 1 g of *resorcinol R*. To 0.5 g of the mixture in a crucible add 0.15 mL of *sulfuric acid R* and heat gently. A dark red semi-solid mass is formed. Add the mass, with care, to 100 mL of *water R*. An orange-yellow colour develops and the solution shows no fluorescence.

C. The filtrate obtained during preparation of the test solution in identification test A gives reaction (a) of iron (*2.3.1*).

TESTS

Solution S. Dissolve 2.0 g in a mixture of 10 mL of *lead-free hydrochloric acid R* and 80 mL of *water R*, heating slightly if necessary. Allow to cool, filter if necessary and dilute to 100 mL with *water R*.

Sulfates (*2.4.13*): maximum 0.2 per cent.

Heat 0.15 g with 8 mL of *dilute hydrochloric acid R* and 20 mL of *distilled water R*. Cool in iced water, filter and dilute to 30 mL with *distilled water R*.

Arsenic (*2.4.2, Method A*): maximum 5 ppm.

Mix 1.0 g with 15 mL of *water R* and 15 mL of *sulfuric acid R*. Warm to precipitate the fumaric acid completely. Cool and add 30 mL of *water R*. Filter. Wash the precipitate with *water R*. Dilute the combined filtrate and washings to 125 mL with *water R*. 25 mL of the solution complies with the test.

Ferric ion: maximum 2.0 per cent.

In a flask with a ground-glass stopper, dissolve 3.0 g in a mixture of 10 mL of *hydrochloric acid R* and 100 mL of *water R* by heating rapidly to boiling. Boil for 15 s. Cool rapidly, add 3 g of *potassium iodide R*, stopper the flask and allow to stand protected from light for 15 min. Add 2 mL of *starch solution R* as indicator. Titrate the liberated iodine with *0.1 M sodium thiosulfate*. Carry out a blank test. The difference between the volumes used in the 2 titrations corresponds to the amount of iodine liberated by ferric ion.

1 mL of *0.1 M sodium thiosulfate* is equivalent to 5.585 mg of ferric ion.

Cadmium: maximum 10 ppm.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. Solution S.

Reference solutions. Prepare the reference solutions using *cadmium standard solution (0.1 per cent Cd) R* and diluting with a 10 per cent *V/V* solution of *lead-free hydrochloric acid R*.

Source: cadmium hollow-cathode lamp.

Wavelength: 228.8 nm.

Atomisation device: air-acetylene flame.

Chromium: maximum 200 ppm.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. Solution S.

Reference solutions. Prepare the reference solutions using *chromium standard solution (0.1 per cent Cr) R* and diluting with a 10 per cent *V/V* solution of *lead-free hydrochloric acid R*.

Source: chromium hollow-cathode lamp.

Wavelength: 357.9 nm.

Atomisation device: air-acetylene flame.

Lead: maximum 20 ppm.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. Solution S.

Reference solutions. Prepare the reference solutions using *lead standard solution (10 ppm Pb) R* and diluting with a 10 per cent *V/V* solution of *lead-free hydrochloric acid R*.

Source: lead hollow-cathode lamp.

Wavelength: 283.3 nm.

Atomisation device: air-acetylene flame.

Mercury: maximum 1 ppm.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. Solution S.

Reference solutions. Prepare the reference solutions using *mercury standard solution (10 ppm Hg) R* and diluting with a 25 per cent *V/V* solution of *lead-free hydrochloric acid R*.

Source: mercury hollow-cathode lamp.

Wavelength: 253.7 nm.

Following the recommendations of the manufacturer, introduce 5 mL of solution S or 5 mL of the reference solutions into the reaction vessel of the cold-vapour mercury assay accessory, add 10 mL of *water R* and 1 mL of *stannous chloride solution R1*.

Nickel: maximum 200 ppm.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. Solution S.

Reference solutions. Prepare the reference solutions using *nickel standard solution (10 ppm Ni) R* and diluting with a 10 per cent *V/V* solution of *lead-free hydrochloric acid R*.

Source: nickel hollow-cathode lamp.

Wavelength: 232 nm.

Atomisation device: air-acetylene flame.

Zinc: maximum 500 ppm.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. Solution S diluted to 10 volumes.

Reference solutions. Prepare the reference solutions using *zinc standard solution (10 ppm Zn) R* and diluting with a 1 per cent *V/V* solution of *lead-free hydrochloric acid R*.

Source: zinc hollow-cathode lamp.

Wavelength: 213.9 nm.

Atomisation device: air-acetylene flame.

Loss on drying (*2.2.32*): maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

ASSAY

Dissolve with slight heating 0.150 g in 7.5 mL of *dilute sulfuric acid R*. Cool and add 25 mL of *water R*. Add 0.1 mL of *ferroin R*. Titrate immediately with *0.1 M cerium sulfate* until the colour changes from orange to light bluish-green.

1 mL of *0.1 M cerium sulfate* is equivalent to 16.99 mg of $C_4H_2FeO_4$.

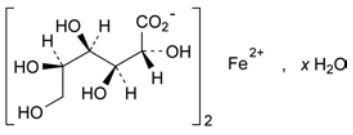
STORAGE

In an airtight container, protected from light.

01/2009:0493

FERROUS GLUCONATE

Ferrosi gluconas



$C_{12}H_{22}FeO_{14}xH_2O$ M_r 446.1 (anhydrous substance)

DEFINITION

Iron(II) di(D-gluconate).

Content: 11.8 per cent to 12.5 per cent of iron(II) (dried substance). It contains a variable amount of water.

CHARACTERS

Appearance: greenish-yellow or grey powder or granules.

Solubility: freely but slowly soluble in water giving a greenish-brown solution, more readily soluble in hot water, practically insoluble in ethanol (96 per cent).

IDENTIFICATION

A. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 20 mg of the substance to be examined in 2 mL of *water R*, heating if necessary in a water-bath at 60 °C.

Reference solution. Dissolve 20 mg of *ferrous gluconate CRS* in 2 mL of *water R*, heating if necessary in a water-bath at 60 °C.

Plate: *TLC silica gel G plate R*.

Mobile phase: *concentrated ammonia R, ethyl acetate R, water R, ethanol (96 per cent) R* (10:10:30:50 *V/V/V/V*).

Application: 5 µL.

Development: over a path of 10 cm.

Drying: at 100-105 °C for 20 min.

Detection: allow to cool and spray with a 50 g/L solution of *potassium dichromate R* in a 40 per cent *m/m* solution of *sulfuric acid R*.

Results: after 5 min, the principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

B. 1 mL of solution S (see Tests) gives reaction (a) of iron (*2.3.1*).

TESTS

Solution S. Dissolve 5.0 g in *carbon dioxide-free water R* prepared from *distilled water R* and heated to about 60 °C, allow to cool and dilute to 50 mL with *carbon dioxide-free water R* prepared from *distilled water R*.

Appearance of solution. The solution is clear (*2.2.1*).

Dilute 2 mL of solution S to 10 mL with *water R*. Examine the solution against the light.

pH (*2.2.3*): 4.0 to 5.5 for solution S, measured 3-4 h after preparation.

Sucrose and reducing sugars. Dissolve 0.5 g in 10 mL of warm *water R* and add 1 mL of *dilute ammonia R1*. Pass *hydrogen sulfide R* through the solution and allow to stand for 30 min. Filter and wash the precipitate with 2 quantities, each of 5 mL, of *water R*. Acidify the combined filtrate and washings to *blue litmus paper R* with *dilute hydrochloric acid R* and add 2 mL in excess. Boil until the vapour no longer darkens *lead acetate paper R* and continue boiling, if necessary, until the volume is reduced to about 10 mL. Cool, add 15 mL of *sodium carbonate solution R*, allow to stand for 5 min and filter. Dilute the filtrate to 100 mL with *water R*. To 5 mL of this solution add 2 mL of *cupri-tartaric solution R* and boil for 1 min. Allow to stand for 1 min. No red precipitate is formed.

Chlorides (*2.4.4*): maximum 0.06 per cent.

Dilute 0.8 mL of solution S to 15 mL with *water R*.

Oxalates. Dissolve 5.0 g in a mixture of 10 mL of *dilute sulfuric acid R* and 40 mL of *water R*. Shake the solution with 50 mL of *ether R* for 5 min. Separate the aqueous layer and shake it with 20 mL of *ether R* for 5 min. Combine the ether layers, evaporate to dryness and dissolve the residue in 15 mL of *water R*. Filter, boil the filtrate until the volume is reduced to 5 mL and add 1 mL of *dilute acetic acid R* and 1.5 mL of *calcium chloride solution R*. Allow to stand for 30 min. No precipitate is formed.

Sulfates (*2.4.13*): maximum 500 ppm.

To 3.0 mL of solution S add 3 mL of *acetic acid R* and dilute to 15 mL with *distilled water R*. Examine the solutions against the light.

Arsenic (*2.4.2, Method A*): maximum 2 ppm, determined on 0.5 g.

Barium. Dilute 10 mL of solution S to 50 mL with *distilled water R* and add 5 mL of *dilute sulfuric acid R*. Allow to stand for 5 min. Any opalescence in the solution is not more intense than that in a mixture of 10 mL of solution S and 45 mL of *distilled water R*.