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Minerals Capsules

DEFINITION

Minerals Capsules contain two or more minerals derived from substances generally recognized as safe, furnishing two or more of the following elements in ionizable form: boron, calcium, chromium, copper, fluorine, iodine, iron, magnesium, manganese, molybdenum, nickel, phosphorus, potassium, selenium, tin, vanadium, and zinc. Capsules contain NLT 90.0% and NMT 125.0% of the labeled amounts of calcium (Ca), copper (Cu), iron (Fe), magnesium (Mg), manganese (Mn), phosphorus (P), potassium (K), and zinc (Zn); and NLT 90.0% and NMT 160.0% of the labeled amounts of boron (B), chromium (Cr), fluorine (F), iodine (I), molybdenum (Mo), nickel (Ni), selenium (Se), tin (Sn), and vanadium (V). They contain no vitamins. They may contain other labeled added substances in amounts that are unobjectionable.

STRENGTH

[NOTE—In the following assays, where more than one assay method is given for an individual ingredient, the requirements may be met by following any one of the specified methods, the method used being stated in the labeling only if *Method 1* is not used. Commercially available atomic absorption standard solutions for the minerals, where applicable, may be used where preparation of a *Standard stock solution* is described in the following assays. Use deionized water where water is specified. Where atomic absorption spectrophotometry is specified in the assay, the concentrations of the *Standard solutions* and the *Sample solutions* may be modified to fit the linear or working range of the instrument.]

• CALCIUM, *Method 1*

Lanthanum chloride solution: 267 mg/mL of lanthanum chloride heptahydrate in 0.125 N hydrochloric acid

Calcium standard solution: 400 µg/mL of calcium. Dissolve 1.001 g of calcium carbonate, previously dried at 300° for 3 h and cooled in a desiccator for 2 h. Dissolve in 25 mL of 1 N hydrochloric acid. Boil to expel carbon dioxide, and dilute with water to 1000 mL.

Standard stock solution: 100 µg/mL of calcium from the *Calcium standard solution* diluted with 0.125 N hydrochloric acid

Standard solutions: Into separate 100-mL volumetric flasks pipet 1.0, 1.5, 2.0, 2.5, and 3.0 mL of the *Standard stock solution*. To each flask add 1.0 mL of *Lanthanum chloride solution*, and dilute with water to volume to obtain concentrations of 1.0, 1.5, 2.0, 2.5, and 3.0 µg/mL of calcium.

Polysorbate 80 solution: Dilute polysorbate 80 with alcohol (1 in 10)

Sample solution: Transfer 5 Capsules to a 100-mL volumetric flask. [NOTE—For hard gelatin Capsules, weigh NLT 20 Capsules. Open the Capsules, without loss of shell material, and transfer the contents to a suitable container. Remove any contents adhering to the empty shells by washing with several portions of ether. Discard the washings, and allow the Capsule shells to dry. Weigh the empty Capsule shells, calculate the net weight of the Capsule contents, and transfer a portion of the Capsule contents, equivalent to 5 Capsules, to a 100-mL volumetric flask.] Add 15 mL of water, 10 mL of 6 N hydrochloric acid, and 1 mL of *Polysorbate 80 solution* to the flask. Heat on a hot plate or steam bath, with intermittent swirling, until the Capsules are completely disintegrated or the contents are dissolved. Boil gently for an additional 15 min. Cool, dilute with water to volume, and filter, discarding the first 5 mL of the filtrate. Dilute this solution with 0.125 N hydrochloric acid to obtain a concentration of 2 µg/mL of calcium, adding 1 mL of *Lanthanum chloride solution* per 100 mL of the final volume.

Instrumental conditions

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

Mode: Atomic absorption spectrophotometry

Lamp: Calcium hollow-cathode

Flame: Nitrous oxide–acetylene

Analytical wavelength: Calcium emission line at 422.7 nm

Blank: 0.125 N hydrochloric acid containing 1 mL of *Lanthanum chloride solution* per 100 mL

Analysis

Samples: *Standard solutions* and *Sample solution*

Determine the absorbances of the solutions against the *Blank*. Plot the absorbances of the *Standard solutions* versus the concentration, in µg/mL, of calcium, and draw the straight line best fitting the five plotted points. From the graph so obtained, determine the concentration, *C*, in µg/mL, of calcium in the *Sample solution*.

Calculate the percentage of the labeled amount of calcium (Ca) in the portion of Capsules taken:

$$\text{Result} = (C/C_U) \times 100$$

C = measured concentration of calcium in the *Sample solution* (µg/mL)

C_U = nominal concentration of calcium in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–125.0% of the labeled amount of calcium (Ca)

• **CHROMIUM, Method 1**

Chromium standard solution: 1000 µg/mL of chromium from potassium dichromate, previously dried at 120° for 4 h, in water. Store in a polyethylene bottle.

Standard stock solution: 10 µg/mL of chromium from the *Chromium standard solution* diluted with 6 N hydrochloric acid and water (1 in 20)

Standard solutions: Transfer 10.0 and 20.0 mL of the *Standard stock solution* to separate 100-mL volumetric flasks, and transfer 15.0 and 20.0 mL of the *Standard stock solution* to separate 50-mL volumetric flasks. Dilute the contents of each of the four flasks with 0.125 N hydrochloric acid to volume to obtain concentrations of 1.0, 2.0, 3.0, and 4.0 µg/mL of chromium.

Sample solution: Proceed as directed in *Calcium, Method 1*, except prepare the *Sample solution* to contain 1 µg/mL of chromium and omit the use of the *Lanthanum chloride solution*.

Instrumental conditions

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

Mode: Atomic absorption spectrophotometry

Lamp: Chromium hollow-cathode

Flame: Air–acetylene

Analytical wavelength: Chromium emission line at 357.9 nm

Blank: 0.125 N hydrochloric acid

Analysis

Samples: *Standard solutions* and *Sample solution*

Determine the absorbances of the solutions against the *Blank*. Plot the absorbances of the *Standard solutions* versus the concentration, in µg/mL, of chromium, and draw the straight line best fitting the four plotted points. From the graph so obtained, determine the concentration, C , in µg/mL, of chromium in the *Sample solution*.

Calculate the percentage of the labeled amount of chromium (Cr) in the portion of Capsules taken:

$$\text{Result} = (C/C_U) \times 100$$

C = measured concentration of chromium in the *Sample solution* (µg/mL)

C_U = nominal concentration of chromium in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–160.0% of the labeled amount of chromium (Cr)

• **COPPER, Method 1**

Copper standard solution: Dissolve 1.00 g of copper foil in a minimum volume of a 50% (v/v) solution of nitric acid, and dilute with a 1% (v/v) solution of nitric acid to 1000 mL. This solution contains 1000 µg/mL of copper.

Standard stock solution: 100 µg/mL of copper from the *Copper standard solution* diluted with 0.125 N hydrochloric acid

Standard solutions: To separate 200-mL volumetric flasks transfer 1.0, 2.0, 4.0, 6.0, and 8.0 mL of the *Standard stock solution*. Dilute with water to volume to obtain concentrations of 0.5, 1.0, 2.0, 3.0, and 4.0 µg/mL of copper.

Sample solution: Proceed as directed in *Calcium, Method 1*, except prepare the *Sample solution* to contain 2 µg/mL of copper and omit the use of the *Lanthanum chloride solution*.

Instrumental conditions

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

Mode: Atomic absorption spectrophotometry

Lamp: Copper hollow-cathode

Flame: Air–acetylene

Analytical wavelength: Copper emission line at 324.7 nm

Blank: 0.125 N hydrochloric acid

Analysis

Samples: *Standard solutions* and *Sample solution*

Determine the absorbances of the solutions against the *Blank*. Plot the absorbances of the *Standard solutions* versus the concentration, in µg/mL, of copper, and draw the straight line best fitting the five plotted points. From the graph so obtained, determine the

concentration, C , in $\mu\text{g/mL}$, of copper in the *Sample solution*.

Calculate the percentage of the labeled amount of copper (Cu) in the portion of Capsules taken:

$$\text{Result} = (C/C_U) \times 100$$

C = measured concentration of copper in the *Sample solution* ($\mu\text{g/mL}$)

C_U = nominal concentration of copper in the *Sample solution* ($\mu\text{g/mL}$)

Acceptance criteria: 90.0%–125.0% of the labeled amount of copper (Cu)

• **FLUORIDE, Method 1**

[NOTE—Store all solutions in plastic containers.]

3 M sodium acetate solution: Dissolve 408 g of sodium acetate in 600 mL of water in a 1000-mL volumetric flask. Allow the solution to equilibrate to room temperature, and dilute with water to volume. Adjust with a few drops of acetic acid to a pH of 7.0.

Sodium citrate solution: Dissolve 222 g of sodium citrate in 250 mL of water in a 1000-mL volumetric flask. Add 28 mL of perchloric acid, and dilute with water to volume.

Fluoride standard stock solution: 500 $\mu\text{g/mL}$ of fluoride from a quantity of sodium fluoride, previously dried at 100° for 4 h and cooled in a desiccator, in water

Intermediate stock solution A: 100 $\mu\text{g/mL}$ of fluoride from *Fluoride standard stock solution* diluted with water

Intermediate stock solution B: 10 $\mu\text{g/mL}$ of fluoride from *Fluoride standard stock solution* diluted with water

Standard solutions: To five separate 100-mL volumetric flasks transfer 3.0, 5.0, and 10.0 mL of *Intermediate stock solution B* and 5.0 and 10.0 mL of *Intermediate stock solution A*. To each flask add 10.0 mL of 1 N hydrochloric acid, 25 mL of 3 M sodium acetate solution, and 25.0 mL of *Sodium citrate solution*. Dilute the contents of each flask with water to volume to obtain concentrations of 0.3, 0.5, 1.0, 5.0, and 10.0 $\mu\text{g/mL}$ of fluoride.

Sample solution: Remove the contents of Capsules by cutting open the Capsules. Mix, and determine the weight of the contents. Transfer a quantity of the mixed Capsule contents, equivalent to 200 μg of fluoride, to a 100-mL volumetric flask. Add 10.0 mL of 1 N hydrochloric acid, 25.0 mL of 3 M sodium acetate solution, and 25.0 mL of *Sodium citrate solution*. Dilute with water to volume.

Analysis

Samples: *Standard solutions* and *Sample solution*

To separate plastic beakers, each containing a plastic-coated stirring bar, transfer 50.0 mL each of the *Standard solutions* and the *Sample solution*. Measure the potentials (see [pH \(791\)](#)), in mV, of the *Standard solutions* and the *Sample solution*, with a pH meter capable of a minimum reproducibility of ± 0.2 mV and equipped with a fluoride-specific ion-indicating electrode and a calomel-reference electrode. [NOTE—When taking measurements, immerse the electrodes in the solution, stir on a magnetic stirrer with an insulated top until equilibrium is attained (1–2 min), and record the potential. Rinse and dry the electrodes between measurements, taking care to avoid damaging the crystal of the specific-ion electrode.]

Plot the logarithms of fluoride concentrations, in $\mu\text{g/mL}$, of the *Standard solutions* versus the potential, in mV. From the standard response curve so obtained and the measured potential of the *Sample solution*, determine the concentration, C , in $\mu\text{g/mL}$, of fluoride in the *Sample solution*.

Calculate the percentage of the labeled amount of fluorine (F) in the portion of Capsules taken:

$$\text{Result} = (C/C_U) \times 100$$

C = measured concentration of fluoride in the *Sample solution* ($\mu\text{g/mL}$)

C_U = nominal concentration of fluorine in the *Sample solution* ($\mu\text{g/mL}$)

Acceptance criteria: 90.0%–160.0% of the labeled amount of fluorine (F)

• **FLUORIDE, Method 2**

[NOTE—Use plastic containers and deionized water throughout this procedure.]

pH 10.0 buffer: Add 214 mL of 0.1 N sodium hydroxide to 1000 mL of 0.05 M sodium bicarbonate.

Mobile phase: Alcohol, 0.1 N sulfuric acid, and water (20:5:175)

Standard stock solution: 220 $\mu\text{g/mL}$ of [USP Sodium Fluoride RS](#) in water. This solution contains 100 $\mu\text{g/mL}$ of fluoride.

Standard solution

[NOTE—Condition the solid-phase extraction column specified for use in the *Standard solution* and *Sample solution* in the following manner.

Using a vacuum at a pressure not exceeding 5 mm of mercury, wash the column with 1 column volume of methanol followed by 1 column volume of *pH 10.0 buffer*. Do not allow the column top to dry. If the top of the column becomes dry, recondition the column.]

Transfer 10.0 mL of the *Standard stock solution* to a 100-mL volumetric flask. Add 75 mL of water, and adjust with 0.1 N sodium hydroxide to a pH of 10.4 ± 0.1 . Dilute with water to volume. Filter, discarding the first 15 mL of the filtrate. Transfer 25.0 mL of the filtrate to a 50-

mL volumetric flask. Add 15.0 mL of water, and adjust with 0.1 N sodium hydroxide to a pH of 10.0. Dilute with *pH 10.0 buffer* to volume. Elute a portion of this solution through a 3-mL solid-phase extraction column containing L1 packing that is connected through an adaptor to a second solid-phase extraction column containing sulfonylpropyl strong cation-exchange packing. Discard the first 3 mL of the eluate, and collect the rest of the eluate in a suitable flask for injection into the chromatograph.

Sample solution: Weigh NLT 20 Capsules in a tared weighing bottle. Open the Capsules, without loss of shell material, and transfer the contents to a 100-mL container. If necessary, remove any contents adhering to the empty shells by washing with several portions of ether. Discard the washings, and dry the Capsule shells with the aid of a current of dry air. Weigh the empty Capsule shells in the tared weighing bottle, and calculate the net weight of the Capsule contents. Transfer a portion of the Capsule contents, equivalent to a nominal amount of 1 mg of fluorine, to a 100-mL volumetric flask. Add 15 mL of water, and shake vigorously. Rinse the sides of the flask with 15 mL of water, and allow to stand for 10 min. Dilute with water to 85 mL, adjust with 1 N sodium hydroxide to a pH of 10.4 ± 0.1 , and dilute with water to 100 mL. Proceed as directed in *Standard solution*, beginning with "Filter, discarding the first 15 mL of the filtrate."

Chromatographic system

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

Mode: LC

Detector: Conductivity

Columns

Guard: 4.6-mm × 3-cm; packing L17

Analytical: 7.8-mm × 30-cm; packing L17

Flow rate: 0.5 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Measure the peak areas of fluoride.

Calculate the percentage of the labeled amount of fluorine (F) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

C_S = concentration of fluoride in the *Standard solution* (µg/mL)

C_U = nominal concentration of fluorine in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–160.0% of the labeled amount of fluorine (F)

• IODIDE

Bromine water: To 20 mL of bromine in a glass-stoppered bottle add 100 mL of water. Insert the stopper into the bottle, and shake. Allow to stand for 30 min, and use the supernatant.

Analysis: Remove the contents of Capsules by cutting open the Capsules. Mix, and determine the weight of the contents. Transfer a quantity of the contents, equivalent to 3 mg of iodine, to a nickel crucible. Add 5 g of sodium carbonate, 5 mL of 50% (w/v) sodium hydroxide solution, and 10 mL of alcohol, taking care that the entire specimen is moistened. Heat the crucible on a steam bath to evaporate the alcohol, then dry the crucible at 100° for 30 min to prevent spattering upon subsequent heating. Transfer the crucible with its contents to a furnace heated to 500°, and heat the crucible for 15 min. [NOTE—Heating at 500° is necessary to carbonize any organic matter present; a higher temperature may be used, if necessary, to ensure complete carbonization of all organic matter.] Cool the crucible, add 25 mL of water, cover the crucible with a watchglass, and boil gently for 10 min. Filter the solution, and wash the crucible with boiling water, collecting the filtrate and washings in a beaker. Add phosphoric acid until the solution is neutral to methyl orange, then add 1 mL excess of phosphoric acid. Add excess of *Bromine water*, and boil the solution gently until colorless and then for 5 min longer. Add a few crystals of salicylic acid, and cool the solution to 20°. Add 1 mL of phosphoric acid and 0.5 g of potassium iodide, and titrate the liberated iodine with 0.005 N sodium thiosulfate VS, adding starch TS when the liberated iodine color has nearly disappeared. Calculate the percentage of the labeled amount of iodine (I) in the portion of Capsules taken:

$$\text{Result} = V \times N_A \times F \times I_{me} \times (A_W/W) \times (100/L)$$