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Fish Oil Containing Omega-3 Acids Capsules

DEFINITION

Fish Oil Containing Omega-3 Acids Capsules contain NLT 95.0% and NMT 105.0% of the labeled amount of Fish Oil Containing Omega-3 Acids where Fish Oil Containing Omega-3 Acids is the purified, winterized, and deodorized fatty oil obtained from fish of the families Engraulidae, Carangidae, Clupeidae, Osmeridae, Scombridae, and Ammodytidae. The omega-3 acids are defined as the following: alpha-linolenic acid (C18:3 n-3), moroctic acid (C18:4 n-3), eicosatetraenoic acid (C20:4 n-3), eicosapentaenoic acid (EPA) (C20:5 n-3), heneicosapentaenoic acid (C21:5 n-3), docosapentaenoic acid (C22:5 n-3), and docosahexaenoic acid (DHA) (C22:6 n-3). It contains NLT 28.0% (w/w) of total omega-3 acids, expressed as free acids, consisting of NLT 13.0% of EPA and NLT 9.0% of DHA. Suitable antioxidants in appropriate concentrations may be added.

IDENTIFICATION

• **A.** The oil contained in the Capsules meet the requirements for the following test. The retention times of the docosahexaenoic acid methyl ester and eicosapentaenoic acid methyl ester peaks from *Test solution 1* in *Content of EPA and DHA* correspond to those of the docosahexaenoic acid methyl ester and eicosapentaenoic acid methyl ester peaks from *Standard solution 2a* and *Standard solution 2b*, respectively, in [Fats and Fixed Oils \(401\), Procedures, Omega-3 Fatty Acids Determination and Profile, Content of EPA and DHA](#). The sum of the areas for EPA and DHA methyl esters is NLT 22% of the total detected area for the methyl esters, and no other peak in the chromatogram has an area higher than 20% of the total detected area for the methyl esters. In addition to the EPA and DHA peaks, *Test solution 1* exhibits at least 15 more peaks with retention times similar to those of the *Fish oil standard solution*, as obtained in the test for *Content of EPA and DHA*.

STRENGTH

• CONTENT OF FISH OIL

Analysis: Weigh NLT 10 Capsules in a tared weighing bottle; carefully open the Capsules, without loss of shell material; and transfer the combined Capsule contents to a 100-mL beaker. Remove any adhering substance from the emptied Capsules by washing with several small portions of [2,2,4-trimethylpentane](#). Discard the washings, and allow the empty Capsules to dry in a current of dry air until the 2,2,4-trimethylpentane is completely evaporated. Weigh the empty Capsules in the original tared weighing bottle, and calculate the average net weight per Capsule.

Acceptance criteria: 95.0%–105.0% of the labeled amount

• CONTENT OF EPA AND DHA

(See [Fats and Fixed Oils \(401\), Procedures, Omega-3 Fatty Acids Determination and Profile](#).)

System suitability solution 1, System suitability solution 2, Standard solution 1a, Standard solution 1b, Standard solution 2a, Standard solution 2b, Test solution 1, Test solution 2, Chromatographic system, System suitability, and Analysis: Proceed as directed in [Fats and Fixed Oils \(401\), Procedures, Omega-3 Fatty Acids Determination and Profile, Content of EPA and DHA](#), for triglycerides.

Fish oil standard solution: Transfer 300 mg of [USP Fish Oil RS](#) into a 10-mL volumetric flask, and dissolve in and dilute with *Antioxidant Solution* to volume. Proceed as directed for *Test Solution 1 (for triglycerides)* in [Fats and Fixed Oils \(401\), Procedures, Omega-3 Fatty Acids Determination and Profile, Content of EPA and DHA](#), starting with "Transfer 2.0 mL".

Identify the relevant fatty acid methyl esters in the *Fish oil standard solution* by comparing their retention times with those in the reference chromatogram supplied with the [USP Fish Oil RS](#).

Calculate the percentage of EPA and DHA in the portion of fish oil containing omega-3 acids taken from the Capsules.

Acceptance criteria: NLT 13.0% (w/w) of EPA and NLT 9.0% (w/w) of DHA

• CONTENT OF TOTAL OMEGA-3 ACIDS

(See [Fats and Fixed Oils \(401\), Procedures, Omega-3 Fatty Acids Determination and Profile](#).)

Analysis: Proceed as directed in [Fats and Fixed Oils \(401\), Procedures, Omega-3 Fatty Acids Determination and Profile, Content of EPA and DHA, Content of total omega-3 acids \(for triglycerides\)](#).

Acceptance criteria: NLT 28.0% (w/w) of total omega-3 acids, expressed as free acids

PERFORMANCE TESTS

• [DISINTEGRATION AND DISSOLUTION OF DIETARY SUPPLEMENTS \(2040\), Rupture Test for Soft-Shell Capsules](#): Meet the requirements

• [WEIGHT VARIATION OF DIETARY SUPPLEMENTS \(2091\)](#): Meet the requirements

CONTAMINANTS

Change to read:

• **LIMIT OF ARSENIC**

[NOTE—For the preparation of all aqueous solutions and for the rinsing of glass, polytetrafluoroethylene, and plastic vessels before use, use water that has first been passed through a strong-acid, strong-base, mixed-bed ion-exchange resin. Select all reagents to have as low a content of arsenic as practicable, and store all reagent solutions in containers of borosilicate glass. Cleanse glass, polytetrafluoroethylene, and plastic vessels before use by soaking them in warm 8 N [nitric acid](#) for 30 min and by rinsing them with deionized water.]

1% Palladium stock solution: Transfer 1 g of ultrapure palladium metal into a Teflon beaker. Add 20 mL of [water](#) and 10 mL of [nitric acid](#), and warm on a hot plate to dissolve. Allow the solution to cool to room temperature, transfer into a 100-mL volumetric flask, and dilute with deionized water to volume.

1% Magnesium nitrate stock solution: Transfer 1 g of ultrapure magnesium nitrate to a Teflon beaker. Add 40 mL of [water](#) and 1 mL of [nitric acid](#), and warm on a hot plate to dissolve the solids. Allow the solution to cool to room temperature, transfer to a 100-mL volumetric flask, and dilute with deionized water to volume.

Modifier working solution: 1% *Palladium stock solution*, 1% *Magnesium nitrate stock solution*, and 2% [nitric acid](#) (3:2:5). A volume of 5 µL provides 0.015 mg of palladium and 0.01 mg of magnesium nitrate.

Blank: [Nitric acid](#) and [water](#) (5 in 100)

Standard stock solution: Transfer 10.0 mL of *Standard Arsenic Solution*, prepared as directed in the test for [▲Arsenic \(211\), Procedures, Procedure 1](#) ▲ (CN 1-Jun-2023), to a 100-mL volumetric flask. Add 40 mL of [water](#) and 5 mL of [nitric acid](#), and dilute with [water](#) to volume. This solution contains 0.10 µg/mL of arsenic.

Standard solutions: Dilute the *Standard stock solution* with the *Blank* to obtain concentrations of 0.002, 0.005, 0.010, 0.025, and 0.050 µg/mL of arsenic.

Sample solution: For the preparation of the *Sample solution*, use a microwave oven with a magnetron frequency of 2455 MHz and a selectable output power of 0–950 W in 1% increments, equipped with advanced composite vessels with 100-mL polytetrafluoroethylene liners. Use rupture membranes to vent vessels should the pressure exceed 125 psi. The vessels fit into a turntable, and each vessel can be vented into an overflow container. Equip the microwave oven with an exhaust tube to ventilate fumes. [CAUTION—Wear proper eye protection and protective clothing and gloves.] Transfer approximately 500 mg from content of Capsules, weighed to the nearest 0.1 mg, into a Teflon digestion vessel liner. Prepare samples in duplicate. Add 15 mL of [nitric acid](#), and swirl gently. Cover the vessels with lids, leaving the vent fitting off. Predigest overnight under a hood. Place the rupture membrane in the vent fitting, and tighten the lid. Place all vessels on the microwave oven turntable. Connect the vent tubes to the vent trap, and connect the pressure-sensing line to the appropriate vessel. Initiate a two-stage digestion procedure by heating the microwave at 15% power for 15 min, followed by 25% power for 45 min. Remove the turntable of vessels from the oven, and allow the vessels to cool to room temperature. [NOTE—A cool water bath may be used to speed the cooling process.] Vent the vessels when they reach room temperature. Remove the lids, and slowly add 2 mL of 30% hydrogen peroxide to each. Allow the reactions to subside, and seal the vessels. Return the vessels on the turntable to the microwave oven, and heat for an additional 15 min at 30% power. Remove the vessels from the oven, and allow them to cool to room temperature. Transfer the cooled digests into 25-mL volumetric flasks, and dilute with [water](#) to volume.

Analysis: Program the graphite furnace as follows. Dry at 115° using a 1-s ramp, a 65-s hold, and an argon flow of 300 mL/min. Char the sample at 1000° using a 1-s ramp, a 20-s hold, and an airflow of 300 mL/min. Cool down, and purge the air from the furnace for 10 s by using a 20° set temperature and an argon flow of 300 mL/min. Atomize at 2400° using a 0-s ramp and a 5-s hold with the argon flow stopped. Clean out at 2600° using a 1-s ramp and a 5-s hold. Separately inject equal volumes (20 µL) of the *Blank*, the *Standard solutions*, and the *Sample solution*, followed by a 5-µL injection of the *Modifier working solution* for each of the samples, into the graphite tube of a suitable graphite furnace atomic absorption spectrometer equipped with a hollow-cathode lamp for arsenic. Determine the peak area at the arsenic emission line at 193.7 nm, corrected for background absorption. Plot the corrected peak areas of the *Standard solutions* versus their contents of arsenic, in µg/mL, and calculate the regression line best fitting the points. Determine the concentration, *C*, in µg/mL, of arsenic in each mL of the *Sample solution* by interpolation from the regression line.

Calculate the content of arsenic in the portion of Capsules taken:

$$\text{Result} = (C/W) \times 25$$

C = concentration of arsenic in each mL of the *Sample solution* (µg/mL)

W = weight of fish oil containing omega-3 acids taken to prepare the *Sample solution* (g)

Acceptance criteria: NMT 0.1 µg/g

• LIMIT OF LEAD

[NOTE—For the preparation of all aqueous solutions and for the rinsing of glass, polytetrafluoroethylene, and plastic vessels before use, use water that has first been passed through a strong-acid, strong-base, mixed-bed ion-exchange resin. Select all reagents to have as low a content of lead as practicable, and store all reagent solutions in containers of borosilicate glass. Cleanse glass, polytetrafluoroethylene, and plastic vessels before use by soaking them in warm 8 N [nitric acid](#) for 30 min and by rinsing them with deionized water.]

10% Monobasic ammonium phosphate solution: 10 g of ultrapure monobasic ammonium phosphate in 1 mL of [nitric acid](#) and 40 mL of [water](#) to dissolve the phosphate. Dilute with deionized water to 100 mL.

1% Magnesium nitrate solution: Transfer 1 g of ultrapure magnesium nitrate to a Teflon beaker. Add 40 mL of [water](#) and 1 mL of [nitric acid](#), and warm on a hot plate to dissolve the solids. Allow the solution to cool to room temperature, transfer to a 100-mL volumetric flask, and dilute with deionized water to volume.

Modifier working solution: 10% *Monobasic ammonium phosphate solution*, 1% *Magnesium nitrate solution*, and 2% [nitric acid](#) (2:1:2). A volume of 5 µL provides 0.2 mg of phosphate plus 0.01 mg of magnesium nitrate.