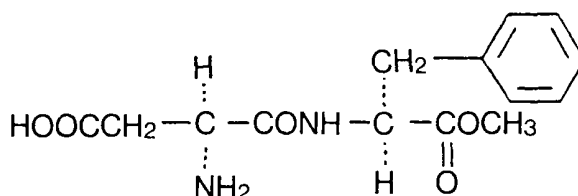


D. MONOGRAPHS

Aspartame

L- -Aspartyl-L-phenylalanine Methyl Ester



C₁₄H₁₈N₂O₅

Mol. Wt. 294.31

Content Aspartame, when calculated on the dried basis, contains 98.0 - 102.0% of aspartame (C₁₄H₁₈N₂O₅).

Description Aspartame occurs as a white crystalline powder or granules. It is odorless and has a strong sweet taste.

Identification (1) Determine the infrared absorption spectrum of Aspartame as directed in the Potassium Bromide Disk Method under the Infrared Spectrophotometry and compare the obtained spectrum with the Reference Spectrum of aspartame. Both spectra exhibit similar intensities of absorption at the same wave numbers.

Purity (1) Specific rotation [α]_D²⁰: +14.5 - +16.5° (2 g, 15 mol/l formic acid, 50 ml, on the dried basis). Measure within 30 minutes.

(2) Clarity and color of solution Colorless and clear (0.20 g, hydrochloric acid (1 : 60) 20 ml).

(3) pH 4.5 - 6.0.

Test Solution Weigh 1.0 g of Aspartame, and dissolve in water to make 125 ml.

(4) Heavy metals Not more than 10 μg/g as Pb (2.0 g, Method 2, Control solution Lead Standard Solution 2.0 ml).

(5) Arsenic Not more than 4.0 μg/g as As₂O₃ (0.50 g, Method 1, Apparatus B).

(6) 5-Benzyl-3,6-dioxo-2-piperazine acetic acid Not more than 1.5% as 5-benzyl-3,6-dioxo-2-piperazine acetic acid.

Test Solution Weigh 10 mg of Aspartame, place into a test tube with a stopper, add 1.0 ml of silylation TS, stopper, and shake. Heat at 80 °C for 30 minutes, shake for 15 seconds, allow to cool.

Control Solution Measure separately 3.0 ml of a solution of 5-benzyl-3,6-dioxo-2-piperazine acetic acid in methanol (1 : 20,000), place into a test tube with a stopper, evaporate to dryness on a water bath, add 1.0 ml of silylation TS to the residue, and proceed in the same manner as for the sample.

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Measure 3.0 μl each of the test solution and the control solution, and perform Gas Chromatography under the operating conditions given below. The peak height of the 5-benzyl-3,6-dioxo-2-piperazine acetic acid of the test solution does not exceed the peak height of the 5-benzyl-3,6-dioxo-2-piperazine acetic acid of the control solution.

Operating conditions

Detector: Hydrogen flame ionization detector.

Column packing material

Liquid phase: 3% Methylsilicon polymer of the amount of support.

Support: 149- to 177- μm diatomaceous earth for gas chromatography.

Column tube: Glass or stainless steel tube 2 m in length and 3 - 4 mm in internal diameter.

Column temperature: Constant temperature of 195 - 205 .

Carrier gas and flow rate: Use helium or nitrogen. Adjust the flow rate so that 5-benzyl-3,6-dioxo-2-piperazine acetic acid appears about 7 - 9 minutes after the injection.

(7) Other optical isomers Not more than 0.04% as L-
-aspartyl-D-phenylalanine methyl ester.

Test Solution Weigh 0.5 g of Aspartame, dissolve in citrate buffer (pH 2.2) to make 100 ml, and use this solution as the test solution.

Control Solution Measure 10 ml of L- -aspartyl-D-phenylalanine methyl ester solution (1 : 50,000), add citrate buffer (pH 2.2) to make 100 ml.

Measure equal amounts of the test solution and the control solution, and perform Liquid Chromatography under the operating conditions given below, using an amino acid automatic analyzer. The peak height of the L- -aspartyl-D-phenylalanine methyl ester of the test solution does not exceed the peak height of the L- -aspartyl-D-phenylalanine methyl ester of the control solution.

Operating conditions

Detector: Visible range absorption detector (measurement wavelength: 570 nm).

Column packing material: 17- μm gel-form strongly acidic cation-exchange resin.

Column tube: Glass tube 55 cm in length and 9 mm in internal diameter.

Column temperature: 55 .

Mobile phase: Citrate buffer (pH 5.28).

Flow rate: 1 ml/min.

Reaction coil: Teflon tube 29 m in length and 0.5 mm in internal diameter.

Reaction chamber temperature: 100 .

Flow rate of ninhydrin - ethylene glycol monomethyl ether TS: 0.5 ml/min.

Amount of test solution and control solution injected: Constant amount of 50 - 500 μl .

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Loss on Drying Not more than 4.5% (105 °C, 4 hours).

Residue on Ignition Not more than 0.20%

Assay Weigh accurately 0.3 g of Aspartame, dissolve in 3 ml of formic acid, add 50 ml of acetic acid, and immediately titrate with 0.1 mol/l perchloric acid. For confirmation of endpoint, use usually potentiometer. When 0.5 ml of 2,6-dimethyl-4-naphtholbenzein is used as an indicator, the endpoint is when the brown color of the solution changes to green. Perform a blank test in the same manner, and make any necessary correction. Calculate on the dried basis.

1 ml of 0.1 mol/l perchloric acid = 29.431 mg of $C_{24}H_{42}O_7$