

Choline Chloride

C₅H₁₄ClNO 139.62

(2-Hydroxyethyl)trimethylammonium chloride.

2-Hydroxy-N,N,N,-trimethylethanaminium chloride.

Choline Chloride contains not less than 99.0 percent and not more than 100.5 percent of C₅H₁₄ClNO, calculated on the anhydrous basis.

Packaging and storage— Preserve in well-closed containers.

Identification—

A: [Infrared Absorption](#) [197K](#) .

B: A solution (1 in 20) meets the requirements of the tests for [Chloride](#) [191](#) .

[pH](#) [791](#) : between 4.0 and 7.0, in a solution (1 in 10).

[Water, Method I](#) [921](#) : not more than 0.5%.

[Residue on ignition](#) [281](#) : not more than 0.05%.

[Arsenic, Method I](#) [211](#) — Add 30 mL of water and 5 mL of hydrochloric acid to dissolve the sample: the limit is 2 µg per g.

[Lead](#) [251](#) — [note—Use methylene chloride in place of chloroform to prepare the Dithizone Extraction Solution and Standard Dithizone Solution.]

Ammonium hydroxide–sodium hydroxide solution— Transfer 8.4 g of sodium hydroxide solution (1 in 2) to a plastic bottle, add 100 mL of ammonium hydroxide, and mix.

Standard solution— Transfer 1.0 mL of the Diluted Standard Lead Solution to a separatory funnel containing 25.0 mL of water.

Test solution— Dissolve 3.00 g in a separatory funnel containing 25.0 mL of water.

Procedure— Separately add 6.0 mL of Ammonium Citrate Solution and 3.0 mL of Potassium Cyanide Solution to the Standard solution and the Test solution. Extract each of the resulting solutions three times with 5.0-mL portions of Dithizone Extraction Solution, shaking for 60 seconds and draining off each extract into another separator. Shake the combined dithizone solutions for 30 seconds with 20.0 mL of nitric acid (1 in 100), and discard the methylene chloride

layer. Add 6.0 mL of Ammonia Cyanide Solution, 2 mL of Ammonium hydroxide–sodium hydroxide solution, and 10 mL of Standard Dithizone Solution, and shake for 45 seconds. Allow the phases to separate, and measure the absorbance of the lower layer at 510 nm with a suitable spectrophotometer. The absorbance of the Test solution is not more than the absorbance of the Standard solution: not more than 0.3 µg per g is found.

[Heavy metals, Method II](#) [231](#) : 0.001%.

Limit of total amines—

Standard solution— Dissolve an accurately weighed quantity of trimethylamine hydrochloride in water, and dilute quantitatively, and stepwise if necessary, to obtain a solution having a known concentration of 500 µg per mL.

Test solution— Transfer 10.0 g of Choline Chloride to a beaker containing a plastic-coated stirring bar, add 170 mL of water and 30.0 mL of [sodium hydroxide TS](#), and stir until dissolved.

System suitability solution— Dissolve an accurately weighed quantity of trimethylamine hydrochloride in water, and dilute quantitatively, and stepwise if necessary, to obtain a solution containing 10 µg of trimethylamine hydrochloride per mL. Transfer 10.0 mL of this solution to a beaker containing a plastic-coated stirring bar, add 170 mL of water and 30.0 mL of [sodium hydroxide TS](#), and stir until dissolved.

Electrode system— Use a gas-sensing, ammonia-specific indicating electrode with internal reference connected to a pH meter capable of measuring potentials with a minimum reproducibility of ± 0.1 mV (see [pH](#) [791](#)).

Standard response line— Transfer 30.0 mL of [sodium hydroxide TS](#) to a suitable beaker, and add enough water to give a total volume of 200 mL. Add a plastic-coated stirring bar, insert the electrode into the solution, and record the potential, in mV. Continue stirring, and at 5-minute intervals add 0.200, 0.600, 1.00, and 2.00 mL of Standard solution, and record the potential after each addition. Plot the logarithms of the cumulative trimethylamine concentrations (0.50, 1.50, 2.50, and 5.00 µg per mL) versus potential, in mV, and determine the slope (S) of the Standard response line for the electrode.

System suitability— Proceed with the System suitability solution as directed for Test solution in the Procedure, and measure the potentials: the trimethylamine equivalent is between 8.5 and 11.5 mg per L.

Procedure— Rinse the electrode, insert it into the Test solution, stir, and record the potential, in mV. Add 0.100 mL of the Standard solution, and record the potential. Add another 0.100 mL of the Standard solution, and record the potential. [note—If the total change after the second addition of the Standard solution is less than 10 mV, add a third aliquot of 0.200 mL.] Calculate the quantity, in µg per g, of total amines in the portion of Choline Chloride taken by the formula:

$$500VA / (F - 1)W$$

in which VA is the total volume of the Standard solution added to the Test solution; W is the weight, in g, of Choline Chloride taken to prepare the Test solution; and the correction factor, F, is calculated by the formula:

$$\text{antilog} [(mVF - mV0) / S]$$

in which mVF is the final reading, in mV, after the additions of the Standard solution; mV0 is the initial reading, in mV, of the Test solution; and S is the slope of the Standard response line for the electrode: not more than 0.001% is found.

Chromatographic purity—

Buffer solution— Dissolve 7.1 g of anhydrous dibasic sodium phosphate in 1 L of water. Adjust with phosphoric acid to a pH of 2.5.

Mobile phase— Prepare a filtered and degassed mixture of Buffer solution and acetonitrile (70:30).

Standard solution— Transfer an accurately weighed amount, not more than 100 mg, of [USP Choline Chloride RS](#) to a 24-mL screw-capped vial, and add 400 mg of 3,5-dinitrobenzoyl chloride and 10 mL of acetonitrile. Cap the vial, heat to 55 °C, and continue heating for 2 hours. Cool to room temperature, and add 5 mL of water. Allow to stand for 5 minutes. Quantitatively transfer the solution to a 25-mL volumetric flask, dilute with acetonitrile to volume, and mix. Dilute a volume of this solution with Mobile phase to obtain a solution having a known concentration of 2.0 µg of [USP Choline Chloride RS](#) per mL.

Test solution— Transfer about 110 mg of Choline Chloride, accurately weighed, to a 24-mL screw-capped vial. Dry at 120 °C for 2 hours. Add 400 mg of 3,5-dinitrobenzoyl chloride and 10 mL of acetonitrile. Cap the vial, heat to 55 °C, and continue heating for 2 hours. Cool to room temperature, and add 5 mL of water. Allow to stand for 5 minutes. Quantitatively transfer the solution to a 50-mL volumetric flask, dilute with Mobile phase to volume, and mix. Pipet 2.0 mL of the solution to a 25-mL volumetric flask, dilute with Mobile phase to volume, and mix.

Chromatographic system— The liquid chromatograph is equipped with a 208-nm detector and a 4.6-mm × 25-cm column that contains packing L7. The column temperature is maintained at 30 °C. The flow rate is about 1.0 mL per minute. Chromatograph the Standard solution, and record the peak responses as directed for Procedure: the capacity factor, k' , is not less than 2; and the relative standard deviation determined from the choline chloride derivative peak is not more than 5%.

Procedure— Separately inject equal volumes (about 20 µL) of the Standard solution and the Test solution into the chromatograph, record the chromatograms, and measure all the peak responses. Calculate the percentage of each impurity in the portion of Choline Chloride taken by the formula:

$$62,500(C/W)(r_i / r_S)$$

in which C is the concentration, in mg per mL, of [USP Choline Chloride RS](#) in the Standard solution; W is the weight, in mg, of Choline Chloride taken to prepare the Test solution; r_i is the peak response for each impurity, other than that for the choline chloride derivative and 3,5-dinitrobenzoic acid obtained from the Test solution; and r_S is the peak response for the choline chloride derivative obtained from the Standard solution: not more than 0.3% of any individual impurity is found; and not more than 2.0% of total impurities is found.

Residual solvents : meets the requirements, except that the limit for 1,4-dioxane is 10 µg per g.

Assay— Transfer an accurately weighed quantity of Choline Chloride, about 120 mg, to a conical flask, dissolve in 35 mL of water, and add 3 drops of acetic acid. Titrate with 0.1 N silver nitrate VS, determining the endpoint potentiometrically (see [Titrimetry](#) [541](#)). Perform a blank determination, and make any necessary correction. Each mL of 0.1 N silver nitrate is equivalent to 13.96 mg of C₅H₁₄ClNO.