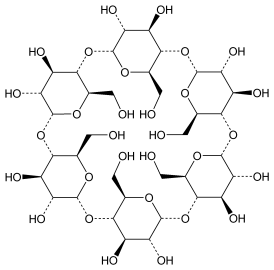
Alfadex



$(C_6H_{10}O_5)_6$ 972.84
Alpha cyclodextrin [*10016-20-3*].

» Alfadex is composed of six alpha-(1-4) linked D-glucopyranosyl units. It contains not less than 98.0 percent and not more than 101.0 percent of $(C_6H_{10}O_5)_6$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers. No storage requirements specified.

USP Reference standards ⟨11⟩**—***USP Alpha Cyclodextrin RS*. *USP Beta Cyclodextrin RS*. *USP Gamma Cyclodextrin RS*.

Clarity of solution—Dissolve 1.0 g in 100.0 mL of previously boiled and cooled water: the resulting solution is clear.

Identification—

A: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

B: It meets the requirements of the test for *Specific rotation* ⟨781S⟩.

C: Mix 0.2 g with 2 mL of iodine TS, warm in a water bath to dissolve the test specimen, and allow to stand at room temperature: a yellow-brown precipitate is formed.

Specific rotation ⟨781S⟩**:** between +147° and +152°, determined at 20°.

Test solution: 10 mg per mL, in water.

Microbial limits ⟨61⟩**—**It meets the requirements of the tests for absence of *Salmonella* species and *Escherichia coli*. The total aerobic bacterial count does not exceed 1000 cfu per g. The total combined molds and yeasts count does not exceed 100 cfu per g.

pH ⟨791⟩**—**The pH of the mixture of 30 mL of its aqueous solution (1 in 100) and 1 mL of *Potassium chloride solution* is 5.0 to 8.0.

Potassium chloride solution—Transfer 22.4 g of potassium chloride into a 100-mL volumetric flask, and dilute with water to volume.

Water, *Method I* ⟨921⟩**:** not more than 11.0%.

Residue on ignition ⟨281⟩**:** not more than 0.1%, determined on 1.0 g.

Heavy metals, *Method II* ⟨231⟩**:** 10 µg per g.

Reducing sugars—

Cupric solution—Dissolve 15 g of cupric sulfate in water to make 100 mL.

Tartrate solution—Dissolve 2.5 g of anhydrous sodium carbonate, 2.5 g of potassium sodium tartrate, 2.0 g of sodium bicarbonate, and 20 g of anhydrous sodium sulfate in water to make 100 mL.

Cupric–tartaric solution—Immediately before use, mix 1 part of *Cupric solution* with 25 parts of *Tartrate solution.*

Ammonium molybdate reagent—Mix 10 mL of a solution of disodium arsenate (6 in 100), 50 mL of a solution of ammonium molybdate (1 in 10), and 90 mL of diluted sulfuric acid, and dilute with water to 200 mL.

Test solution—Transfer about 1.0 g of Alfadex, accurately weighed, and calculated on the anhydrous basis, to a 100-mL volumetric flask, dissolve in and dilute with water that has been previously boiled and cooled to room temperature, to volume, and mix. To 1 mL of this solution add 1 mL of *Cupric–tartaric solution.* Heat on a water bath for 10 minutes, then cool to room temperature. Add 10 mL of *Ammonium molybdate reagent*, and allow to stand for 15 minutes.

Standard solution—Prepare as directed for the *Test solution*, at the same time, except to use 1 mL of a solution containing 20 mg of glucose per L.

Procedure—Concomitantly measure the absorbance of the *Test solution* and the *Standard solution* at the wavelength of maximum absorbance at 740 nm relative to that of water, with a suitable spectrophotometer. The absorbance of the *Test solution* is not greater than that of the *Standard solution* (0.2%).

Related compounds—

System suitability solution—Prepare as directed for *System suitability preparation* in the *Assay*.

Standard solution—Transfer 5.0 mL of the *System suitability solution* into a 50-mL volumetric flask, and dilute with water to volume.

Test solution—Use the *Assay stock preparation* prepared as directed in the *Assay*.

Chromatographic system (see *Chromatography* ⟨621⟩)—Proceed as directed in the *Assay*.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. For the *Test solution*, the areas of any peaks corresponding to beta cyclodextrin or to gamma cyclodextrin are not greater than half of the area of the corresponding peaks in the chromatogram of the *Standard solution* (0.25%), and the sum of the areas of all the peaks, excluding the principal peak and the peaks corresponding to beta cyclodextrin or to gamma cyclodextrin, is not greater than half of the area of the peak corresponding to alpha cyclodextrin in the chromatogram of the *Standard solution* (0.5%).

Light-absorbing impurities—

Test solution—Transfer about 1.0 g of Alfadex, accurately weighed, and calculated on the anhydrous basis, to a 100-mL volumetric flask, dissolve in and dilute with water, which has been previously boiled and cooled to room temperature, to volume, mix, and pass through a 0.2-µm filter.

Procedure—Determine the absorbance of the *Test solution* in a 1-cm cell with a suitable spectrophotometer, after correcting for the blank: between 230 nm and 350 nm, the absorbance is not greater than 0.10; and between 350 nm and 750 nm, the absorbance is not greater than 0.05.

Organic volatile impurities, *Method IV* ⟨467⟩: meets the requirements.

(Official until July 1, 2008)

Assay—

Mobile phase—Prepare a filtered and degassed mixture of water and methanol (90 : 10). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Alpha Cyclodextrin RS in water to obtain a solution having a known concentration of about 1.0 mg per mL, calculated on the anhydrous basis.

System suitability preparation—Dissolve accurately weighed quantities of USP Alpha Cyclodextrin RS, USP Beta Cyclodextrin RS, and USP Gamma Cyclodextrin RS in water to obtain a solution having known concentrations of about 1.0 mg per mL for USP Alpha Cyclodextrin RS, calculated on the anhydrous basis, about 0.5 mg of each per mL for USP Beta Cyclodextrin RS and USP Gamma Cyclodextrin RS, each calculated on the anhydrous basis.

Assay stock preparation—Transfer 250 mg of Alfadex, accurately weighed, and calculated on the anhydrous basis, to a 25-mL volumetric flask, and dissolve in water with the aid of heat. Cool, and dilute with water to volume.

Assay preparation—Transfer 5.0 mL of the *Assay stock preparation* to a 50-mL volumetric flask, and dilute with water to volume.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a refractive index detector and a 4.6-mm × 25-cm column that contains 5-µm packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *System suitability preparation*, and record the chromatograms for about 3.5 times the retention time of alpha cyclodextrin. Record the peak responses as directed for *Procedure:* the resolution, *R*, between the gamma cyclodextrin and alpha cyclodextrin peaks is not less than 1.5; and for the alpha cyclodextrin peak, the relative standard deviation for replicate injections is not more than 2.0%. [NOTE—For the purpose of identification, the relative retention times are about 1.0

for alpha cyclodextrin, about 2.2 for beta cyclodextrin, and about 0.7 for gamma cyclodextrin.]

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of $(C_6H_{10}O_5)_6$ in the portion of Alfadex taken by the formula:

$$2500(C/W)(r_U / r_S)$$

in which C is the concentration, in mg per mL, of alpha cyclodextrin in the *Standard preparation;* W is the weight, in mg, of alpha cyclodextrin taken to prepare the *Assay stock preparation;* and r_U and r_S are the peak responses of the alpha cyclodextrin peak obtained from the *Assay preparation* and the *Standard preparation*, respectively.