SORBITOL

Prepared at the 46th JECFA (1996), published in FNP 52 Add 4 (1996) superseding specifications prepared at the 33rd JECFA (1988), published in FNP 38 (1988). Metals and arsenic specifications revised at the 57th JECFA (2001). An ADI 'Not specified' was established at the 26th JECFA (1982).

SYNONYMS D-Glucitol, D-sorbitol, sorbit, sorbol, INS No. 420(i)

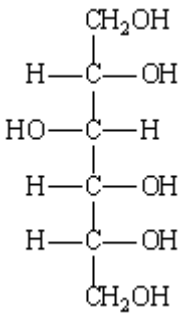
DEFINITION

Chemical names D-Sorbitol

C.A.S. number 50-70-4

Chemical formula $C_6H_{14}O_6$

Structural formula



Formula weight 182.17

Assay Not less than 97.0% of $C_6H_{14}O_6$ of total glycitols and not less than 91.0% of D-sorbitol on the anhydrous basis. The term glycitols refers to compounds with the structural formula CH_2OH-$(CHOH)_n$-CH_2OH, where n is an integer less than or equal to 4.

DESCRIPTION White hygroscopic powder, crystalline powder, flakes or granules

FUNCTIONAL USES Sweetener, humectant, sequestrant, texturizer, stabilizer, bulking agent

CHARACTERISTICS

IDENTIFICATION

Solubility (Vol. 4) Very soluble in water, slightly soluble in ethanol

Melting range (Vol. 4) 88 - 102°

Thin layer chromatography (Vol. 4)	Passes test Proceed as directed under *Thin Layer Chromatography of Polyols* Use the following: Standard solution: Dissolve 50 mg of reference standard sorbitol (available from US Pharmacopeial Convention, Inc. 12601 Twinbrook Parkway, Rockville, MD 20852, USA) in 20 ml water Test solution: Dissolve 50 mg of the sample in 20 ml of water
PURITY	
Water (Vol. 4)	Not more than 1% (Karl Fischer Method)
Sulfated ash (Vol. 4)	Not more than 0.1% Test 2 g of sample (Method I)
Chlorides (Vol. 4)	Not more than 50 mg/kg Test 10 g of sample by the Limit Test using 1.5 ml of 0.01N hydrochloric acid in the control
Sulfates (Vol. 4)	Not more than 100 mg/kg Test 10 g of sample by the Limit Test using 2.0 ml of 0.01N sulfuric acid in the control
Nickel (Vol. 4)	Not more than 2 mg/kg Proceed as directed under *Nickel in Polyols*
Reducing sugars	Not more than 0.3% Proceed as directed under *Reducing Substances (as Glucose*), Method II. The weight of cuprous oxide shall not exceed 50 mg
Total sugars	Not more than 1% (as glucose) Weigh 2.1 g of the sample into a 250 ml flask fitted with a ground glass joint, add 40 ml of 0.1N hydrochloric acid, attach a reflux condenser, and reflux for 4 h. Transfer the solution to a 400 ml beaker, rinsing the flask with about 10 ml of water, neutralize with 6N sodium hydroxide and proceed as directed under *Reducing Substances(as Glucose*) Method II. The weight of the cuprous oxide shall not exceed 50 mg.
Lead (Vol. 4)	Not more than 1 mg/kg Determine using an atomic absorption technique appropriate to the specified level. The selection of sample size and method of sample preparation may be based on the principles of the method described in Volume 4, “Instrumental Methods.”
METHOD OF ASSAY	Determine the polyol content of the sample using *liquid chromatography* (see Volume 4).

Apparatus
Liquid chromatograph (HPLC)
Detection: differential refractometer maintained at constant temperature
Integrator recorder
Column: AMINEX HPX 87 C (or equivalent resin in calcium form), length 30 cm, internal diameter 9 mm
Eluent: double distilled degassed water (filtered through Millipore membrane filter 0.45 µm)
Chromatographic conditions
Column temperature: 85±0.5^{o}
Eluent flow rate: 0.5 ml/min

Standard preparation
Dissolve an accurately weighed quantity of sorbitol in water to obtain a solution having known concentration of about 10.0 mg of sorbitol per ml.

Sample preparation
Transfer about 1 g of the sample accurately weighed to a 50 ml volumetric flask, dilute with water to volume and mix.

Procedure
Separately inject equal volumes (about 20 µl) of the sample preparation and the standard preparation into the chromatograph. Record the chromatograms and measure the responses of each peak. Calculate separately the quantities, in mg, of sorbitol and other glycitols in the portion of sample taken by the following formula:

$$50 \times C \times \frac{R_U}{R_S}$$

in which C is the concentration, in mg per ml, of sorbitol in the standard preparation; R_U is the peak response of the sample preparation and R_S is the peak response of the standard preparation.

Sorbitol Solution

» Sorbitol Solution is an aqueous solution containing not less than 64.0 percent of D-sorbitol ($C_6H_{14}O_6$). The amounts of total sugars, other polyhydric alcohols, and any hexitol anhydrides, if detected, are not included in the requirements nor in the calculated amount under *Other Impurities.*

Packaging and storage—Preserve in well-closed containers. No storage requirements specified.

Change to read:

USP Reference standards ⟨11⟩**—***USP Sorbitol RS.* •*USP Diethylene Glycol RS. USP Ethylene Glycol RS.*• (RB 1-Feb-2010)

Change to read:

Identification—

A: Dissolve 1.4 g of Sorbitol Solution in 75 mL of water. Transfer 3 mL of this solution to a 15-cm test tube, add 3 mL of freshly prepared catechol solution (1 in 10), mix, add 6 mL of sulfuric acid, mix again, and gently heat the tube in a flame for about 30 seconds: a deep pink or wine color appears.

B: 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.*

•C: Limit of Diethylene Glycol and Ethylene Glycol

Diluent: Acetone and water (96 : 4)

Standard solution: 0.08 mg/mL of USP Diethylene Glycol RS and 0.08 mg/mL of USP Ethylene Glycol RS in *Diluent*.

Sample solution: Transfer 2.0 g of Sorbitol Solution to a 25-mL volumetric flask. Add 1.0 mL of *Diluent* to the flask, and vortex the flask for 3 minutes. Add the remaining *Diluent* to the flask to volume in three equal portions. Vortex the flask for about 3 minutes after each addition of *Diluent*. Pass a portion of the supernatant layer obtained through a 0.45-µm nylon filter. Discard the first 2 mL of the filtrate, and collect the rest of the filtrate for analysis. [NOTE—Acetone is used to precipitate sorbitol.]

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 15-m fused-silica capillary column; 0.25-µm layer of phase G46

Temperature

Detector: 300°

Injection port: 240°

Column: See the temperature program table below.

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
70	—	70	2
70	50	300	5

Carrier gas: Helium

Flow rate: 3.0 mL/minute

Injection size: 1.0 µL

Injection type: Split injection. The split ratio is about 10 : 1. [NOTE—A split liner, deactivated with glass wool, is used.]

System suitability

Sample: *Standard solution*

[NOTE—Diethylene glycol elutes after ethylene glycol in the chromatogram.]

Suitability requirements

Resolution: Not less than 30 between ethylene glycol and diethylene glycol

Analysis

Samples: *Standard solution* and *Sample solution*

Based on the *Standard solution*, identify the peaks of ethylene glycol and diethylene glycol. Compare peak areas of ethylene glycol and diethylene glycol in the *Standard solution* and the *Sample solution.*

Acceptance criteria

Diethylene glycol: The peak area of diethylene glycol in the *Sample solution* is not more than the peak area of diethylene glycol in the *Standard solution*, corresponding to not more than 0.10% of diethylene glycol in Sorbitol Solution.

Ethylene glycol: The peak area of ethylene glycol in the *Sample solution* is not more than the peak area of ethylene glycol in the *Standard solution*, corresponding to not more than 0.10% of ethylene glycol in Sorbitol Solution.

• (RB 1-Feb-2010)

pH ⟨791⟩**:** between 5.0 and 7.5, in a 14% (w/w) solution of Sorbitol Solution in carbon dioxide-free water.

Water, *Method I* ⟨921⟩**:** between 28.5% and 31.5%.

Residue on ignition ⟨281⟩**:** not more than 0.1%, calculated on the anhydrous basis, determined on a 2-g portion, accurately weighed.

Reducing sugars—To an amount of Sorbitol Solution, equivalent to 3.3 g on the anhydrous basis, add 3 mL of water, 20.0 mL of cupric citrate TS, and a few glass beads. Heat so that boiling begins after 4 minutes, and maintain boiling for 3 minutes. Cool rapidly, and add 40 mL of diluted acetic acid, 60 mL of water, and 20.0 mL of 0.05 N iodine VS. With continuous shaking, add 25 mL of a mixture of 6 mL of hydrochloric acid and 94 mL of water. When the precipitate has dissolved, titrate the excess of iodine with 0.05 N sodium thiosulfate VS using 2 mL of starch TS, added towards the end of the titration, as an indicator. Not less than 12.8 mL of 0.05 N sodium thiosulfate VS is required, corresponding to not more than 0.3% of reducing sugars, on the anhydrous basis, as glucose. The amount determined in this test is not included in the calculated amount under *Other Impurities.*

Limit of nickel—

Test solution—Dissolve 20.0 g of Sorbitol Solution in diluted acetic acid, and dilute with diluted acetic acid to 100.0 mL. Add 2.0 mL of a saturated ammonium pyrrolidine dithiocarbamate solution (containing about 10 g of ammonium pyrrolidine dithiocarbamate per L) and 10.0 mL of methyl isobutyl ketone, and shake for 30 seconds. Protect from bright light. Allow the two layers to separate, and use the methyl isobutyl ketone layer.

Blank solution—Prepare as directed for *Test solution,* except to omit the use of the Sorbitol Solution.

Standard solutions—Prepare as directed for *Test solution,* except to prepare three solutions by adding 0.5 mL, 1.0 mL, and 1.5 mL of nickel standard solution TS.

Procedure—Set the instrument to zero using the *Blank solution.* Concomitantly determine the absorbances of the *Standard solutions* and the *Test solution* at least three times each, at the wavelength of maximum absorbance at 232.0 nm, with a suitable atomic absorption spectrophotometer (see *Spectrophotometry and Light-Scatter-*

ing ⟨851⟩) equipped with a nickel hollow-cathode lamp and an air–acetylene flame. Record the average of the steady readings for each of the *Standard solutions* and the *Test solution.* Between each measurement, aspirate the *Blank solution,* and ascertain that the reading returns to zero. Plot the absorbances of the *Standard solutions* and the *Test solution* versus the added quantity of nickel. Extrapolate the line joining the points on the graph until it meets the concentration axis. The distance between this point and the intersection of the axes represents the concentration of nickel in the *Test solution.* Not more than 1 µg per g, calculated on the anhydrous basis, is found.

Assay—

Mobile phase, Resolution solution, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay* under *Sorbitol*.

Assay preparation—Accurately weigh about 0.12 g of Sorbitol Solution, and dissolve in and dilute with water to about 20 g. Accurately record the final solution weight, and mix thoroughly.

Procedure—Proceed as directed in the *Assay* under *Sorbitol.* Calculate the percentage of D-sorbitol ($C_6H_{14}O_6$) in the portion of Sorbitol Solution taken by the formula:

$$100(C_S / C_U)(r_U / r_S)$$

in which C_S is the concentration, in mg per g, of USP Sorbitol RS in the *Standard preparation;* C_U is the concentration, in mg per g, of Sorbitol Solution in the *Assay preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.