MANNITOL

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 30th JECFA (1986)

SYNONYMS D-Mannitol, mannite, INS No. 421

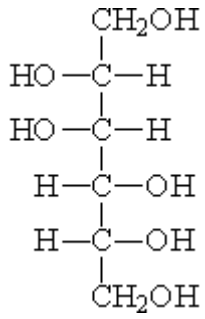
DEFINITION

Chemical names D-Mannitol

C.A.S. number 69-65-8

Chemical formula $C_6H_{14}O_6$

Structural formula



Formula weight 182.17

Assay Not less than 96.0% and not more than 102.0% on the dried basis

DESCRIPTION White, odourless, crystalline powder

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

CHARACTERISTICS

IDENTIFICATION

Solubility (Vol. 4) Soluble in water, very slightly soluble in ethanol; practically insoluble in ether

Melting range (Vol. 4) 164 - 169°

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 mannitol (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	
Loss on drying (Vol. 4)	Not more than 0.3% (105°, 4 h)
Specific rotation (Vol. 4)	[alpha] 20, D: Between +23 and +25° Accurately weigh and dissolve 2.0 g of sample and 2.6 g of disodium tetraborate in about 20 ml of water previously heated to about 30°, shake continuously for 15-30 min without further heating. Dilute the resulting clear solution to 25 ml with water.
pH (Vol. 4)	Between 5 and 8 Add 0.5 ml of a saturated solution of potassium chloride to 10 ml of a 10% w/v solution of the sample, then measure the pH.
Sulfated ash (Vol. 4)	Not more than 0.1% Test 2 g of sample (Method I)
Chlorides (Vol. 4)	Not more than 70 mg/kg Test 10 g of sample by the Limit Test using 2.0 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(Vol. 4)	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(Vol. 4)	Not more than 1.0% (as glucose) Transfer 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 in the *General Method for 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	Determine the mannitol content of the sample using *liquid chromatography*

ASSAY (see Volume 4)

Apparatus
Liquid chromatograph (HPLC)
Detection: differential refractometer maintained at constant temperature
Integrator recorder
Column: AMINEX HPX 87 C (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°
Eluent flow rate: 0.5 ml/min

Standard preparation
Dissolve an accurately weighed quantity of standard reference mannitol in water to obtain a solution having known concentration of about 10.0 mg of mannitol 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 response of the mannitol peak. Calculate the quantity, in mg, of mannitol in the portion of sample taken by the following formula:

$$50 \times C \times \frac{Ru}{Rs}$$

where
C = the concentration, in mg per ml, of mannitol in the standard preparation
R_U = the peak response of the sample preparation
R_S = the peak response of the standard preparation.