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Lactulose Solution

DEFINITION

Lactulose Solution is a solution in water prepared from Lactulose Concentrate. It contains NLT 90.0% and NMT 110.0% of the labeled amount of lactulose ($C_{12}H_{22}O_{11}$).

IDENTIFICATION

- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **B.**

Sample solution: Dilute a portion of Solution with water (1 in 20).

Analysis: Add a few drops of the *Sample solution* to 5 mL of hot alkaline cupric tartrate TS.

Acceptance criteria: A red precipitate of cuprous oxide is formed.

ASSAY

- **Procedure**

Buffer: 1.15 g/L of monobasic sodium phosphate in water

Mobile phase: Acetonitrile and *Buffer* (82:18). Ensure that the concentration of acetonitrile in the *Mobile phase* is between 78% and 85% to obtain appropriate retention times.

Standard solution: 40 mg/mL of USP Lactulose RS, 4.8 mg/mL of USP Anhydrous Lactose RS, and 3.2 mg/mL of USP Epilactose RS in a mixture of acetonitrile and water (1:1)

Sample solution: Nominally equivalent to 40 mg/mL of lactulose prepared as follows. Transfer a quantity of Solution containing 2.0 g of lactulose to a 50-mL volumetric flask, and dissolve in 20 mL of water. Add 25.0 mL of acetonitrile, allow the solution to reach ambient temperature, and dilute with water to volume.

Chromatographic system

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

Mode: LC

Detector: Refractive index

Column: 4.6-mm × 15-cm; 3-µm packing L8

Temperatures

Column: 40 ± 1°

Detector: 40 ± 1°

Flow rate: 1.3 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—The relative retention times are given in *Table 1*.]

Suitability requirements

Resolution: NLT 1.5 between lactulose and lactose; NLT 0.9 between lactulose and epilactose

Relative standard deviation: NMT 2.0% for the main peak

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of lactulose ($C_{12}H_{22}O_{11}$) in the portion of Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Lactulose RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of lactulose in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

• **Uniformity of Dosage Units ⟨905⟩**

Oral Solution packaged in single-unit containers

Acceptance criteria: Meets the requirements

IMPURITIES

• **Organic Impurities**

Buffer, Mobile phase, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*. To evaluate the *Suitability requirements*, use the *Standard solution* prepared as directed in the *Assay*.

Standard solution: 6.4 mg/mL of USP Galactose RS, 4.8 mg/mL of USP Anhydrous Lactose RS, 3.2 mg/mL of USP Epilactose RS, 1.2 mg/mL of USP Tagatose RS, and 0.4 mg/mL of USP Fructose RS in a mixture of acetonitrile and water (1:1)

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentages of galactose, lactose, epilactose, tagatose, and fructose, if found, in the portion of Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of the relevant related compound from the *Sample solution*

r_S = peak response of the relevant related compound from the *Standard solution*

C_S = concentration of the relevant USP Reference Standard in the *Standard solution* (mg/mL)

C_U = nominal concentration of lactulose in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Tagatose	0.30	4
Fructose	0.34	1
Galactose	0.47	16
Epilactose	0.90	8
Lactulose	1.0	—
Lactose	1.17	12

SPECIFIC TESTS

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total bacterial count is NMT 10^2 cfu/g of lactulose, and the tests for *Salmonella* species and *Escherichia coli* are negative.

• **pH ⟨791⟩:** 2.5–6.5, after 15 min of contact with the electrodes

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, preferably at a temperature between 2° and 30°. Avoid subfreezing temperatures.

• **USP Reference Standards ⟨11⟩**

USP Epilactose RS
USP Fructose RS
USP Galactose RS
USP Anhydrous Lactose RS
USP Lactulose RS
USP Tagatose RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
LACTULOSE SOLUTION	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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