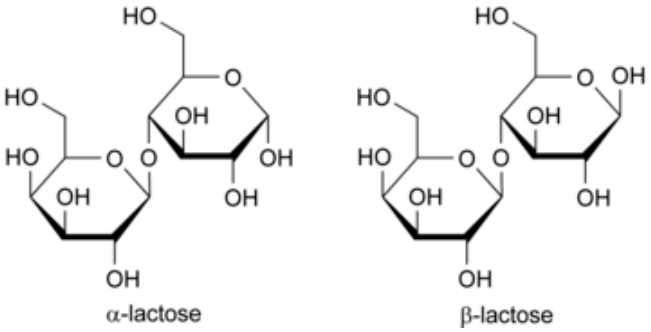
Edition: BP 2025 (Ph. Eur. 11.6 update)

Lactose[1]

General Notices

Anhydrous Lactose

(Ph. Eur. monograph 1061)



$C_{12}H_{22}O_{11}$ 342.3 *63-42-3*

Action and use

Excipient.

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DEFINITION

O-β-D-Galactopyranosyl-(1→4)-β-D-glucopyranose or mixture of *O*-β-D-galactopyranosyl-(1→4)-α-D-glucopyranose and *O*-β-D-galactopyranosyl-(1→4)-β-D-glucopyranose.

♦ CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Freely soluble in water, practically insoluble in ethanol (96 per cent).♦

IDENTIFICATION

First identification: A, ◊ D.

Second identification: B, C, D.◊

A. Infrared absorption spectrophotometry (2.2.24).

Comparison *anhydrous lactose CRS*.

◊ B. Thin-layer chromatography (2.2.27).

Solvent mixture *water R*, *methanol R* (40:60 *V/V*).

Test solution Dissolve 10 mg of the substance to be examined in the solvent mixture and dilute to 20 mL with the solvent mixture.

Reference solution Dissolve 10 mg of *anhydrous lactose CRS* in the solvent mixture and dilute to 20 mL with the solvent mixture.

Plate *TLC silica gel plate R*.

Mobile phase *water R*, *methanol R*, *glacial acetic acid R*, *methylene chloride R* (10:15:25:50 *V/V/V/V*); measure the volumes accurately, as a slight excess of water produces cloudiness.

Application 2 µL; thoroughly dry the points of application.

Development A Over 3/4 of the plate.

Drying A In a current of warm air.

Development B Immediately, over 3/4 of the plate, after renewing the mobile phase.

Drying B In a current of warm air.

Detection Spray with a solution of 0.5 g of *thymol R* in a mixture of 5 mL of *sulfuric acid R* and 95 mL of *ethanol (96 per cent) R*; heat at 130 °C for 10 min.

Results The principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

C. Dissolve 0.25 g in 5 mL of *water R*. Add 5 mL of *ammonia R* and heat in a water-bath at 80 °C for 10 min. A red colour develops.
D. Water (see Tests).◊

TESTS

Solution S

Dissolve 1.0 g in boiling *water R*, allow to cool and dilute to 10.0 mL with *water R*.

Appearance of solution

Solution S is clear (2.2.1) and not more intensely coloured than reference solution BY_7 (*2.2.2, Method II*).

Acidity or alkalinity

Dissolve 6.0 g by heating in 25 mL of *carbon dioxide-free water R*, cool and add 0.3 mL of *phenolphthalein solution R1*. The solution is colourless. Not more than 0.4 mL of *0.1 M sodium hydroxide* is required to change the colour of the indicator to pink or red.

Specific optical rotation (*2.2.7*)

+ 54.4 to + 55.9 (anhydrous substance).

Dissolve 10.0 g in 80 mL of *water R* with heating at 50 °C. Allow to cool and add 0.2 mL of *dilute ammonia R1*. Allow to stand for 30 min and dilute to 100.0 mL with *water R*.

Absorbance: proteins and light-absorbing impurities (*2.2.25*)

Test solution (a) Solution S.

Test solution (b) Dilute 1.0 mL of test solution (a) to 10.0 mL with *water R*.

Spectral range 400 nm for test solution (a) and 210-300 nm for test solution (b).

Results:

— at 400 nm: maximum 0.04 for test solution (a);

— from 210 nm to 220 nm: maximum 0.25 for test solution (b);

— from 270 nm to 300 nm: maximum 0.07 for test solution (b).

Water (*2.5.12*)

Maximum 1.0 per cent, determined on 1.00 g, using a mixture of 1 volume of *formamide R* and 2 volumes of *methanol R* as solvent.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

Microbial contamination

TAMC: acceptance criterion 10^2 CFU/g (*2.6.12*).

Absence of *Escherichia coli* (*2.6.13*).

◊ FUNCTIONALITY-RELATED CHARACTERISTICS

This section provides information on characteristics that are recognised as being relevant control parameters for one or more functions of the substance when used as an excipient (see chapter 5.15). Some of the characteristics described in the Functionality-related characteristics section may also be present in the mandatory part of the monograph since they also represent mandatory quality criteria. In such cases, a cross-reference to the tests described in the mandatory part is included in the Functionality-related characteristics section. Control of the characteristics can contribute to the quality of a medicinal product by improving the consistency of the manufacturing process and the performance of the medicinal product during use. Where control methods are cited, they are recognised as being suitable for the purpose, but

other methods can also be used. Wherever results for a particular characteristic are reported, the control method must be indicated.

The following characteristics may be relevant for lactose used as filler/diluent in solid dosage forms (compressed and powder).

Particle-size distribution (*2.9.31* or *2.9.38*)

Bulk density of powders (*2.9.34*)

α-Lactose and β-lactose

Gas chromatography (*2.2.28*).

Silylation reagent *dimethyl sulfoxide R*, *N-trimethylsilylimidazole R*, *pyridine R* (19.5:22:58.5 *V/V/V*).

Test solution Introduce 10 mg of the substance to be examined into a vial with a screw cap and add 4 mL of the silylation reagent. Sonicate for 20 min at room temperature, allow to cool and transfer 400 µL to an injection vial. Add 1 mL of *pyridine R*, close the vial and mix well.

Reference solution Prepare a mixture of *α-lactose monohydrate R* and *β-lactose R* to obtain an anomeric ratio of about 1:1 based on the labelled anomeric contents of the α-lactose monohydrate and the β-lactose. Introduce 10 mg of the mixture into a vial with a screw cap and add 4 mL of the silylation reagent. Sonicate for 20 min at room temperature, allow to cool, and transfer 400 µL to an injection vial. Add 1 mL of *pyridine R*, close the vial and mix well.

Precolumn:

— *material*: intermediate-polarity deactivated fused silica;

— *size*: *l* = 2 m, Ø = 0.53 mm.

Column:

— *material*: fused silica;

— *size*: *l* = 15 m, Ø = 0.25 mm;

— *stationary phase*: *phenyl(5)methyl(95)polysiloxane R* (film thickness 0.25 µm).

Carrier gas *helium for chromatography R*.

Flow rate 2.8 mL/min.

Temperature:

	Time (min)	Temperature (°C)
Column	0 - 1	80
	1 - 3	80 → 150
	3 - 15.5	150 → 300
	15.5 - 17.5	300
Injection port		275 or use cold on-column injection
Detector		325

Detection Flame ionisation.

Injection 0.5 µL, splitless or by cold on-column injection.

Relative retention With reference to β-lactose (retention time = about 12 min): α-lactose = about 0.9.

System suitability Reference solution:

— *resolution*: minimum 3.0 between the peaks due to α-lactose and β-lactose.

Calculate the percentage content of α-lactose using the following expression:

$$\frac{100 S_a}{S_a + S_b}$$

Calculate the percentage content of β-lactose using the following expression:

$$\frac{100 S_b}{S_a + S_b}$$

S_a = area of the peak due to α-lactose;

S_b = area of the peak due to β-lactose.

Loss on drying (*2.2.32*)

Determine on 1.000 g by drying in an oven at 80 °C for 2 h.◊

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[1] This monograph has undergone pharmacopoeial harmonisation. See chapter *5.8. Pharmacopoeial harmonisation*.