

DEFINITION/CHARACTERS/PRODUCTION

CELLACTOSE 80 is MEGGLE's brand name for a co-processed, directly compressible spray agglomerate comprising 75 % Lactose Monohydrate (Ph. Eur., USP-NF, JP) and 25 % Powdered Cellulose (Ph. Eur., USP-NF, JP). The monographs "Lactose Monohydrate" and "Powdered Cellulose" have undergone pharmacopoeial harmonisation. CELLACTOSE 80 is a white or almost white, odourless powder; partly soluble in water.

Production and release site: Molkerei MEGGLE Wasserburg GmbH & Co. KG (effective July 1st 2020 renamed to MEGGLE GmbH & Co. KG), Megglestr. 6-12, 83512 Wasserburg, Germany

The management system of Molkerei MEGGLE Wasserburg GmbH & Co. KG (effective July 1st 2020 renamed to MEGGLE GmbH & Co. KG), Megglestr. 6-12, 83512 Wasserburg, Germany has been certified meeting the requirements of GMP and GDP according to EXCiPACT™.

Additional regulatory information is available under <https://www.meggle-pharma.com>.

IDENTIFICATION

Method	Specification
Identification CELLACTOSE 80/Ph. Eur. 2.2.24 Infrared absorption spectrophotometry (Annex methods in specification)	conforms
Identification Lactose Monohydrate/Ph. Eur. 2.2.27 Thin-layer chromatographic identification test, modified (Annex methods in specification)	conforms
Identification Powdered Cellulose/Ph. Eur. Powdered Cellulose identification A colour reaction, modified (Annex methods in specification)	conforms
Identification Powdered Cellulose/Sedimentation test (Annex methods in specification)	conforms

TESTS

	Method	Specification
Water	Ph. Eur. 2.5.12 (Annex methods in specification)	4.0 - 7.0 %
Loss on drying	Ph. Eur. 2.2.32 (Annex methods in specification)	max 3.5 %
Sulfated ash	Ph. Eur. 2.4.14 (Annex methods in specification)	max 0.2 %
Lactose Monohydrate calculated on the dried basis	Iodometry (Annex methods in specification)	73.0 - 77.0 %
Powdered Cellulose calculated on the dried basis	Gravimetry (Annex methods in specification)	23.0 - 27.0 %
pH	Ph. Eur. 2.2.3 (Annex methods in specification)	4.0 - 7.0
Particle size distribution < 32 µm	Ph. Eur. 2.9.38/Air-entrainment method (air-jet sieving); 10 g; + 0.1 g Al ₂ O ₃ ; p = 1500 - 2500 Pa; 2 min	max 20 %
Particle size distribution < 160 µm	Ph. Eur. 2.9.38/Air-entrainment method (air-jet sieving); 10 g; + 0.1 g Al ₂ O ₃ ; p = 1500 - 2500 Pa; 2 min	35 - 65 %
Particle size distribution < 250 µm	Ph. Eur. 2.9.38/Air-entrainment method (air-jet sieving); 10 g; + 0.1 g Al ₂ O ₃ ; p = 1500 - 2500 Pa; 2 min	min 80 %

MICROBIAL CONTAMINATION

	Method	Specification
Total aerobic microbial count (TAMC)	Ph. Eur. 2.6.12/USP-NF <61>/JP <4.05>	max 100 cfu/g
Total combined yeasts/moulds count (TYMC)	Ph. Eur. 2.6.12/USP-NF <61>/JP <4.05>	max 50 cfu/g
<i>Escherichia coli</i>	Ph. Eur. 2.6.13/USP-NF <62>/JP <4.05>	absence /10 g
<i>Salmonella</i> spp.	Ph. Eur. 2.6.13/USP-NF <62>/JP <4.05>	absence /10 g

STORAGE

Well-closed container. Storage in an unopened, originally packed MEGGLE container at room temperature under dry and odour-free conditions.

This specification was electronically released.

ANNEX METHODS IN SPECIFICATION

IDENTIFICATION

Identification CELLACTOSE 80 (Ph. Eur. 2.2.24 Infrared absorption spectrophotometry)

The identification is carried out by Infrared absorption (Ph. Eur. 2.2.24). The spectrum of a sample exhibits maxima at the same wavelengths and with the same relative intensities as a 3 + 1 mixture of Lactose Monohydrate (Ph. Eur.) and Powdered Cellulose (Ph. Eur.). Sample preparation is performed by preparation of KBr pellets or direct placing of the sample onto an attenuated reflectance crystal. Spectra are recorded between 4000 and 650 cm⁻¹ (2.5 and 15.4 µm).

Identification Lactose Monohydrate (Ph. Eur. 2.2.27 Thin-layer chromatographic identification test, modified)

Test solution: add 40 mg sample to a mixture of 24 ml water and 36 ml methanol R and stir on a magnetic stirrer for approx. 10 min. Centrifuge the resulting suspension at 3000 rpm. Decant the supernatant and filter through a white ribbon ("Weißband") filter. Use this filtrate for the identification of lactose. Dry the residue from centrifugation for 2 hours at 100 - 105 °C in a drying oven and use this residue for the identification of Powdered Cellulose.

Reference solution (a): Dissolve 10 mg of lactose monohydrate CRS in a mixture of 2 volumes of water R and 3 volumes of methanol R and dilute to 20 ml with the same mixture of solvents.

Reference solution (b): Dissolve 10 mg each of glucose R, lactose R, fructose R and sucrose R in a mixture of 2 volumes of water R and 3 volumes of methanol R and dilute to 20 ml with the same mixture of solvents.

Apply separately to the TLC silica gel plate R 2 µl of each solution and thoroughly dry the starting points. Develop over a path of 15 cm using a mixture of 10 volumes of water R, 15 volumes of methanol R, 25 volumes of anhydrous acetic acid R and 50 volumes of ethylene chloride R. Dry the TLC silica gel plate R in a current of warm air. Repeat the development immediately, after renewing the mobile phase. Dry the TLC silica gel plate R in a current of warm air and spray evenly with a solution of 0.5 g of thymol R in a mixture of 5 ml of sulphuric acid R and 95 ml of alcohol R. Heat at 130 °C for 10 min. 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 reference solution (a). The test is not valid unless the chromatogram obtained with reference solution (b) shows four clearly separated spots.

Identification Powdered Cellulose (Ph. Eur. Powdered Cellulose identification A colour reaction, modified)

The identification of Powdered Cellulose is carried out according to identification test A Ph. Eur.. Place the dried residue obtained from the Test Identification "Lactose Monohydrate" (see above) in a centrifuge tube and disperse in 2 ml of zinc chloride solution R containing iodine. Result: the substance takes on a violett-blue colour.

Identification Powdered Cellulose (Sedimentation test)

Mix 120 g CELLACTOSE 80 with 750 ml water on a magnetic stirrer. Filter the dispersion through a white ribbon ("Weißband") filter and wash with 500 ml water. Complete the filter residue with water to 300 g. The obtained suspension is stirred by

means of a disperser at 18000 rpm for 5 minutes. Transfer 100 ml of the dispersion to a 100 ml graduated cylinder and allow to stand for 1 hour: the Powdered Cellulose settles in the cylinder and a supernatant liquid appears above the layer of the Powdered Cellulose.

TESTS

Water (Ph. Eur. 2.5.12)

Grind CELLACTOSE 80 to a fine powder using a mortar. Add 40 ml formamid/methanol 1:2 (V/V) into a titration flask. Afterwards add approximately 150 mg CELLACTOSE 80 accurately weighed and titrate with an appropriate titrans (e.g. Hydranal-Composite 5).

Loss on drying (Ph. Eur. 2.2.32)

Dry 1.0 - 2.0 g at 80 °C for 2 hours

Sulfated ash (Ph. Eur. 2.4.14)

Determined on 1.0 g

Lactose monohydrate calculated on the dried basis (Iodometry)

Grind CELLACTOSE 80 to a fine powder in a mortar. Afterwards add approximately 260 mg CELLACTOSE 80 accurately weighed into a 250 ml iodine flask and suspend in 90 ml water R. Then add 0.560 g dried anhydrous sodium carbonate and stir until it is dissolved. Add 30 ml iodine solution (0.05 mol/l) with a volumetric pipette. Keep the iodine flask in the dark for 40 minutes at room temperature. Afterwards add 10 ml hydrochloric acid (5 mol/l) and titrate with sodium thiosulfate 0.1 mol/l until the solution turns yellow. Next, add 2.0 ml 1 % starch solution, iodide-free R and titrate until the blue colour disappears. Additionally carry out a blank titration. 1 ml 0.1 M sodium thiosulphate solution is equivalent to 18.02 mg Lactose Monohydrate. Calculate the content of Lactose Monohydrate on the dried basis.

Powdered Cellulose calculated on the dried basis (Gravimetry)

Add 1 to 2 g of the sample accurately weighed to 100 ml of hot dest. water (70 - 80 °C). Stir the mixture for 15 minutes on a magnetic stirrer. Filter the suspension by means of a G4-type glass filter crucible (pore size 10 - 16 µm) which is dried to constant weight and thoroughly tared. Dry the glass filter crucible with the residue at 102 ± 2 °C to constant weight and determine the weight of the residue after cooling in a desiccator. Calculate the content of Powdered Cellulose on the dried basis.

pH (Ph. Eur. 2.2.3)

Shake 5.0 g with 40 ml of carbon dioxide-free water R for 20 min and centrifuge. The pH of the supernatant liquid is determined.

CONTACT

In case of queries please feel free to contact us:

MEGGLE Business Group Excipients & Technology

Telephone: 0049 (0)8071 73 476

Fax: 0049 (0)8071 73 320

Email: service.pharma@meggle.de