

Determination of the content of cyclodextrins

Test method: PML-0700

1. Purpose

This method describes the determination of the content (purity determination) of cyclodextrins.

2. Equipment

The following equipment is needed:

HPLC-equipment, sample vials, ultrasonification bath, 10 ml-volumetric flasks.

3. Chemicals

Cyclodextrin reference standards (prepared by recrystallisation of pharmaceutical grade material from water).

4. Analysis

4.1 Determination of the residual moisture of the cyclodextrin reference standard and sample material: This is done according to PML-0701

4.2 Preparation of the solutions

General remark: for the preparation of solutions it is necessary to use purified deionised water.

1. Sample solution

100.00 mg (95.00 - 105.00 mg) of the sample material are weighed into a 10 ml volumetric flask and filled up with about 8 ml purified deionised water. The volumetric flask is placed into an ultrasonification bath for about 10-15 minutes to achieve complete dissolution of the sample material. After complete dissolution the volumetric flask is filled up to 10.00 ml with purified deionised water (the content of the volumetric flask has to have room temperature!).

2. Reference solution

100.00 mg (95.00 - 105.00 mg) of the reference material are weighed into a 10 ml volumetric flask and filled up with about 8 ml purified deionised water. The volumetric flask is placed into an ultrasonification bath for about 10-15 minutes to achieve complete dissolution of the reference material. After complete dissolution the volumetric flask is filled up to 10.00 ml with purified deionised water (the content of the volumetric flask has to have room temperature!).

4.3 HPLC-analysis

Before performing the analysis the equipment has to be checked for correct function, that means no error message should appear.

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Replaces version: 1	Page 1 of 2	Distribution:QC-Handbook

Aliquots of app. 1 ml of both solutions are pipetted into HPLC-sample vials, are capped and placed into the autosampler tray. From each vial 5 analytical runs are performed.

Parameters for analysis:

Column: Nucleosil-10-NH₂ (Macherey & Nagel Co. D-Düren)

Elution system: acetonitrile/water 67%/33% (volume/volume)

Flow rate: 2 ml/min

Temperature: 40°C

Detection: refractometric detection and integration of peak areas

Injection volume: 9 µl

5. Calculation

From the five analytical runs of each sample the mean value of the peak areas for the reference and the sample are calculated and treated by the following formula:

content in % calculated on dry basis=

$$\frac{F(P) \times m(R) \times (100-WR) \times 100}{F(R) \times m(P) \times (100-WP)}$$

F(P) = Peak area of the sample solution, mean value in area units

F(R) = Peak area of the reference solution, mean value in area units

m(P) = amount of sample in sample solution in mg

m(R) = amount of reference material in reference solution in mg

WR = residual moisture of reference material in %

WP = residual moisture of sample material in %

6. Impurities

By using this method to determine the content of different cyclodextrins it is possible to detect other cyclodextrins in an amount of $\geq 2.0\%$.

Example: in the determination of the content of a gamma-cyclodextrin batch alpha- and beta-cyclodextrin can be detected if the amount of contaminating cyclodextrin is 2.0 % or higher.

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Replaces version: 1	Page 2 of 2	Distribution:QC-Handbook