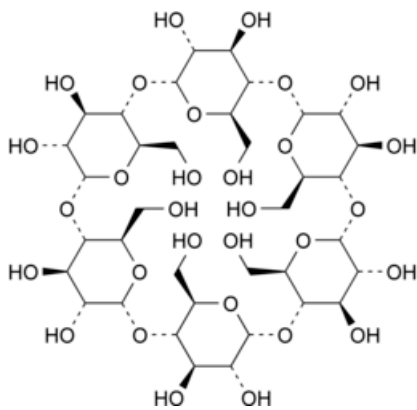| British Pharmacopoeia	Quality standards

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

Alfadex

General Notices

Alphacyclodextrin

(Ph. Eur. monograph 1487)

$[C_6H_{10}O_5]_6$ 973   *10016-20-3*

Action and use

Cyclodextran; carrier molecule for drug delivery systems.

Ph Eur

DEFINITION

Cyclohexakis-(1→4)-(α-D-glucopyranosyl) (cyclomaltohexaose, α-cyclodextrin).

Content

97.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, amorphous or crystalline, hygroscopic powder.

Solubility

Freely soluble in water, slightly soluble in propylene glycol, practically insoluble in anhydrous ethanol and in methylene chloride.

IDENTIFICATION

A. Specific optical rotation (*2.2.7*): + 147 to + 152 (dried substance), determined on solution S (see Tests).
B. Examine the chromatograms obtained in the assay.

Results   The principal peak in the chromatogram obtained with test solution (b) is similar in retention time and size to the principal peak in the chromatogram obtained with reference solution (c).

C.   Dissolve 0.2 g in 2 mL of *iodine solution R4* by warming on a water-bath, and allow to stand at room temperature; a yellowish-brown precipitate is formed.

TESTS

Solution S

Dissolve 1.000 g in *carbon dioxide-free water R* and dilute to 100.0 mL with the same solvent.

Appearance of solution

Solution S is clear (*2.2.1*).

pH (*2.2.3*)

5.0 to 8.0.

Mix 1 mL of a 223.6 g/L solution of *potassium chloride R* and 30 mL of solution S.

Reducing sugars

Maximum 0.2 per cent.

Test solution   To 1 mL of solution S add 1 mL of *cupri-tartaric solution R4*. Heat on a water-bath for 10 min, cool to room temperature. Add 10 mL of *ammonium molybdate reagent R1* and allow to stand for 15 min.

Reference solution   Prepare a reference solution at the same time and in the same manner as the test solution, using 1 mL of a 0.02 g/L solution of *glucose R*.

Measure the absorbance (*2.2.25*) of the test solution and the reference solution at the absorption maximum at 740 nm using *water R* as the compensation liquid. The absorbance of the test solution is not greater than that of the reference solution.

Light-absorbing impurities

Examine solution S between 230 nm and 750 nm. Between 230 nm and 350 nm, the absorbance (*2.2.25*) is not greater than 0.10. Between 350 nm and 750 nm, the absorbance (*2.2.25*) is not greater than 0.05.

Related substances

Liquid chromatography (*2.2.29*).

Test solution (a)   Dissolve 0.250 g of the substance to be examined in *water R* with heating, cool and dilute to 25.0 mL with the same solvent.

Test solution (b)   Dilute 5.0 mL of test solution (a) to 50.0 mL with *water R*.

Reference solution (a)   Dissolve 25.0 mg of <u>betadex CRS</u> (impurity A), 25.0 mg of <u>gammacyclodextrin CRS</u> (impurity B) and 50.0 mg of <u>alfadex CRS</u> in <u>water R</u>, then dilute to 50.0 mL with the same solvent.

Reference solution (b)   Dilute 5.0 mL of reference solution (a) to 100.0 mL with <u>water R</u>.

Reference solution (c)   Dissolve 25.0 mg of <u>alfadex CRS</u> in <u>water R</u> and dilute to 25.0 mL with the same solvent.

Column:

— *size*: l = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: <u>end-capped octadecylsilyl silica gel for chromatography R</u> (5 µm).

Mobile phase   <u>methanol R</u>, <u>water for chromatography R</u> (10:90 *V/V*).

Flow rate   1.5 mL/min.

Detection   Differential refractometer.

Equilibration   With the mobile phase for about 3 h.

Injection   50 µL of test solution (a) and reference solutions (a) and (b).

Run time   3.5 times the retention time of alfadex.

Identification of impurities   Use the chromatogram obtained with reference solution (a) to identify the peaks due to impurities A and B.

Relative retention   With reference to alfadex (retention time = about 6 min): impurity B = about 0.7; impurity A = about 1.7.

System suitability   Reference solution (a):

— <u>resolution</u>: minimum 1.5 between the peaks due to impurity B and alfadex; if necessary, adjust the concentration of methanol in the mobile phase.

Calculation of percentage contents:

— for impurities A and B, use the concentration of the corresponding impurity in reference solution (b);

— for impurities other than A and B, use the concentration of alfadex in reference solution (b).

Limits:

— *impurities A, B*: for each impurity, maximum 0.25 per cent;

— *sum of impurities other than A and B*: maximum 0.5 per cent;

— *reporting threshold*: 0.15 per cent.

Loss on drying (*2.2.32*)

Maximum 11 per cent, determined on 1.000 g by drying in an oven at 120 °C for 2 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modifications.

Injection   Test solution (b) and reference solutions (a) and (c).

System suitability:

— *repeatability*: maximum relative standard deviation of 2.0 per cent for the peak due to alfadex determined on 5 injections of reference solution (a).
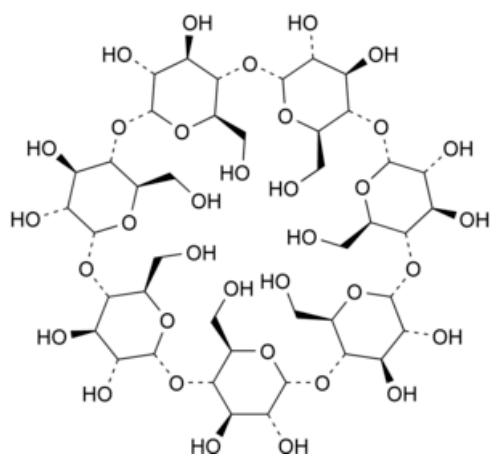
Calculate the percentage content of $[C_6H_{10}O_5]_6$ using the chromatogram obtained with reference solution (c) and taking into account the assigned content of *alfadex CRS*.
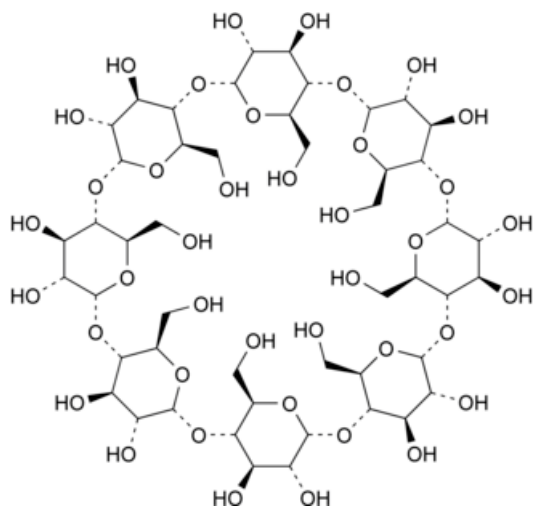
STORAGE

In an airtight container.

IMPURITIES

Specified impurities   A, B.

A.   cycloheptakis-(1→4)-(α-D-glucopyranosyl) (betadex, cyclomaltoheptaose, β-cyclodextrin),

B.   cyclooctakis-(1→4)-(α-D-glucopyranosyl) (gammadex, cyclomaltooctaose, γ-cyclodextrin).

Ph Eur