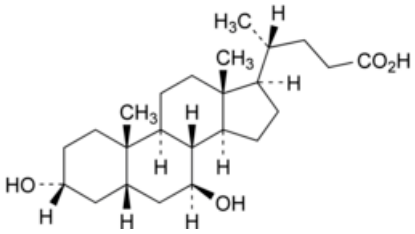
Edition: BP 2025 (Ph. Eur. 11.6 update)

# Ursodeoxycholic Acid

General Notices

*(Ph. Eur. monograph 1275)*



$C_{24}H_{40}O_4$ 392.6 *128-13-2*

**Action and use**

Bile acid; treatment of gallstones.

**Preparations**

Ursodeoxycholic Acid Capsules

Ursodeoxycholic Acid Tablets

Ursodeoxycholic Acid Oral Suspension

Ph Eur

## DEFINITION

3α,7β-Dihydroxy-5β-cholan-24-oic acid.

**Content**

99.0 per cent to 101.0 per cent (dried substance).

## CHARACTERS

**Appearance**

White or almost white powder.

**Solubility**

Practically insoluble in water, freely soluble in ethanol (96 per cent), slightly soluble in acetone, practically insoluble in methylene chloride.

**mp**

About 202 °C.

## IDENTIFICATION

*First identification: A.*

*Second identification: B, C.*

A. Infrared absorption spectrophotometry (2.2.24).

*Comparison* *ursodeoxycholic acid CRS*.

B. Examine the chromatograms obtained in the test for impurity C.

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

C. Dissolve about 10 mg in 1 mL of *sulfuric acid R*. Add 0.1 mL of *formaldehyde solution R* and allow to stand for 5 min. Add 5 mL of *water R*. The suspension obtained is greenish-blue.

## TESTS

**Specific optical rotation** (2.2.7)

+ 58.0 to + 62.0 (dried substance).

Dissolve 0.500 g in *anhydrous ethanol R* and dilute to 25.0 mL with the same solvent.

**Impurity C**

Thin-layer chromatography (2.2.27).

*Solvent mixture* *water R*, *acetone R* (10:90 *V/V*).

*Test solution (a)* Dissolve 0.40 g of the substance to be examined in the solvent mixture and dilute to 10 mL with the solvent mixture.

*Test solution (b)* Dilute 1 mL of test solution (a) to 10 mL with the solvent mixture.

*Reference solution (a)* Dissolve 40 mg of *ursodeoxycholic acid CRS* in the solvent mixture and dilute to 10 mL with the solvent mixture.

*Reference solution (b)* Dissolve 20 mg of *lithocholic acid CRS* (impurity C) in the solvent mixture and dilute to 10.0 mL with the solvent mixture (solution A). Dilute 2.0 mL of this solution to 100.0 mL with the solvent mixture.

*Reference solution (c)* To 5 mL of solution A add 10 mg of *chenodeoxycholic acid CRS* (impurity A) and dilute to 50 mL with the solvent mixture.

*Plate* *TLC silica gel plate R*.

*Mobile phase* *glacial acetic acid R*, *acetone R*, *methylene chloride R* (1:30:60 *V/V/V*).

*Application* 5 µL.

*Development* Over 2/3 of the plate.

*Drying* At 120 °C for 10 min.

*Detection* Spray immediately with a 47.6 g/L solution of *phosphomolybdic acid R* in a mixture of 1 volume of *sulfuric acid R* and 20 volumes of *glacial acetic acid R* and heat at 120 °C until blue spots appear on a lighter background.

*System suitability* Reference solution (c):

— the chromatogram shows 2 clearly separated principal spots.

*Limit* Test solution (a):

— *impurity C*: any spot due to impurity C is not more intense than the principal spot in the chromatogram obtained with reference solution (b) (0.1 per cent).

**Related substances**

Liquid chromatography (2.2.29).

*Solvent mixture* methanol R, mobile phase (10:90 *V/V*).

*Test solution* Dissolve 60 mg of the substance to be examined in the solvent mixture and dilute to 20.0 mL with the solvent mixture.

*Reference solution (a)* Dissolve the contents of a vial of ursodeoxycholic acid for system suitability CRS (containing impurities A and H) in 1.0 mL of the solvent mixture.

*Reference solution (b)* Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

*Column*:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: end-capped octadecylsilyl silica gel for chromatography R (5 µm);

— *temperature*: 40 °C ± 1 °C.

*Mobile phase* Mix 30 volumes of acetonitrile R, 37 volumes of a 0.78 g/L solution of sodium dihydrogen phosphate R adjusted to pH 3 with phosphoric acid R, and 40 volumes of methanol R.

*Flow rate* 0.8 mL/min.

*Detection* Refractometer at 35 ± 1 °C.

*Injection* 150 µL.

*Run time* 4 times the retention time of ursodeoxycholic acid.

*Identification of impurities* Use the chromatogram supplied with ursodeoxycholic acid for system suitability CRS and the chromatogram obtained with reference solution (a) to identify the peaks due to impurities A and H.

*Relative retention* With reference to ursodeoxycholic acid (retention time = about 14 min): impurity H = about 0.9; impurity A = about 2.8.

*System suitability* Reference solution (a):

— resolution: minimum 1.5 between the peaks due to impurity H and ursodeoxycholic acid.

*Limits*:

— *impurity A*: not more than 10 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent);

— *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);

— *total*: not more than 15 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.5 per cent);

— *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

**Loss on drying** (2.2.32)

Maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

**Sulfated ash** (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

## ASSAY

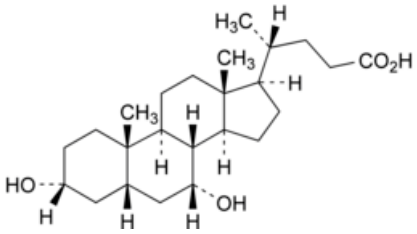
Dissolve 0.350 g in 50 mL of *ethanol (96 per cent) R*, previously neutralised to 0.2 mL of *phenolphthalein solution R*. Add 50 mL of *water R* and titrate with *0.1 M sodium hydroxide* until a pink colour is obtained.

1 mL of *0.1 M sodium hydroxide* is equivalent to 39.26 mg of $C_{24}H_{40}O_4$.

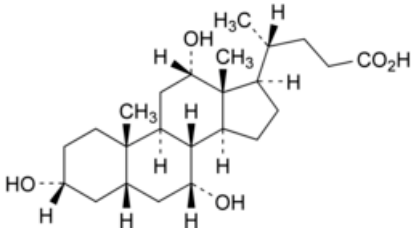
## IMPURITIES

*Specified impurities* A, C.

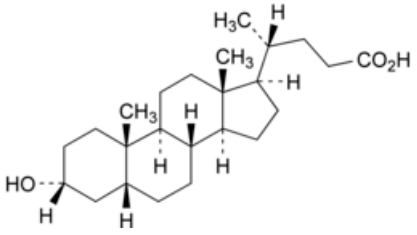
*Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical use (2034). It is therefore not necessary to identify these impurities for demonstration of compliance. See also 5.10. Control of impurities in substances for pharmaceutical use)* B, D, E, F, G, H, I.



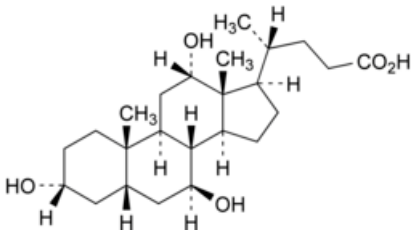
A. 3α,7α-dihydroxy-5β-cholan-24-oic acid (chenodeoxycholic acid),



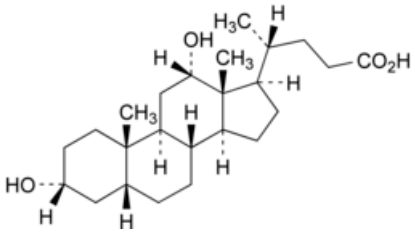
B. 3α,7α,12α-trihydroxy-5β-cholan-24-oic acid (cholic acid),



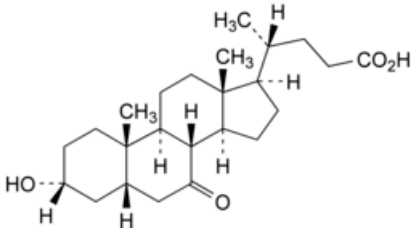
C. 3α-hydroxy-5β-cholan-24-oic acid (lithocholic acid),



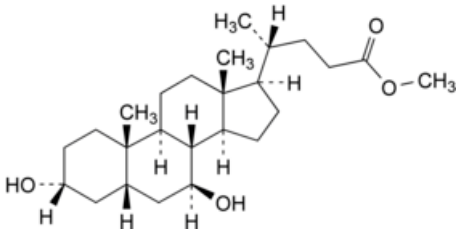
D. 3α,7β,12α-trihydroxy-5β-cholan-24-oic acid (ursocholic acid),



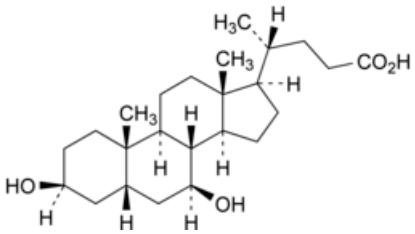
E. 3α,12α-dihydroxy-5β-cholan-24-oic acid (deoxycholic acid),



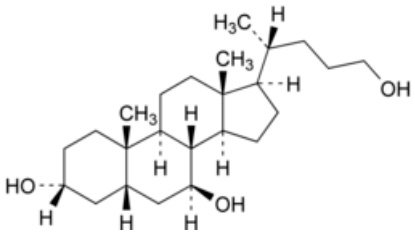
F. 3α-hydroxy-7-oxo-5β-cholan-24-oic acid,



G. methyl 3α,7β-dihydroxy-5β-cholan-24-oate,



H. 3β,7β-dihydroxy-5β-cholan-24-oic acid,




I. 5β-cholane-3α,7β,24-triol.

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