Calculate the percentage content of total triterpenoid derivatives, expressed as asiaticoside, using the following expression:

$$\frac{V}{m}\left[\frac{A+(B\times 1.017)+(C\times 0.526)+(D\times 0.509)}{\overline{\mathrm{RF}}}\right]$$

V = volume of the test solution, in millilitres;

m = mass of the substance to be examined in the test solution, in milligrams;

A = area of the peak due to asiaticoside in the chromatogram obtained with the test solution;

B = area of the peak due to madecassoside in the chromatogram obtained with the test solution;

C = area of the peak due to madecassic acid in the chromatogram obtained with the test solution;

D = area of the peak due to asiatic acid in the chromatogram obtained with the test solution;

$\overline{\mathrm{RF}}$ = mean response factor of asiaticoside.

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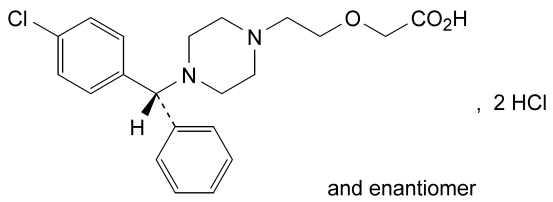
corrected 6.0

CETIRIZINE DIHYDROCHLORIDE

Cetirizini dihydrochloridum



$C_{21}H_{27}Cl_3N_2O_3$ M_r 461.8
[83881-52-1]

DEFINITION

(*RS*)-2-[2-[4-[(4-Chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetic acid dihydrochloride.

Content: 99.0 per cent to 100.5 per cent (dried substance).

CHARACTERS

Appearance: white or almost white powder.

Solubility: freely soluble in water, practically insoluble in acetone and in methylene chloride.

IDENTIFICATION

First identification: B, D.

Second identification: A, C, D.

A. Ultraviolet and visible absorption spectrophotometry (*2.2.25*).

Test solution. Dissolve 20.0 mg in 50 ml of a 10.3 g/l solution of *hydrochloric acid R* and dilute to 100.0 ml with the same acid. Dilute 10.0 ml of the solution to 100.0 ml with a 10.3 g/l solution of *hydrochloric acid R*.

Spectral range: 210-350 nm.

Absorption maximum: at 231 nm.

Specific absorbance at the absorption maximum: 359 to 381.

B. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *cetirizine dihydrochloride CRS*.

C. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 10 mg of the substance to be examined in *water R* and dilute to 5 ml with the same solvent.

Reference solution (a). Dissolve 10 mg of *cetirizine dihydrochloride CRS* in *water R* and dilute to 5 ml with the same solvent.

Reference solution (b). Dissolve 10 mg of *chlorphenamine maleate CRS* in *water R* and dilute to 5 ml with the same solvent. To 1 ml of the solution add 1 ml of reference solution (a).

Plate: *TLC silica gel GF_{254} plate R.*

Mobile phase: *ammonia R, methanol R, methylene chloride R* (1:10:90 *V/V/V*).

Application: 5 µl.

Development: over 2/3 of the plate.

Drying: in a current of cold air.

Detection: examine in ultraviolet light at 254 nm.

System suitability: reference solution (b):

– the chromatogram obtained shows 2 clearly separated spots.

Results: the principal spot in the chromatogram obtained with the test solution is similar in position and size to the principal spot in the chromatogram obtained with reference solution (a).

D. It gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 20 ml with the same solvent.

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*).

pH (*2.2.3*): 1.2 to 1.8 for solution S.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 20.0 mg of the substance to be examined in the mobile phase and dilute to 100.0 ml with the mobile phase.

Reference solution (a). Dissolve 5.0 mg of *cetirizine dihydrochloride CRS* and 5.0 mg of *cetirizine impurity A CRS* in the mobile phase and dilute to 25.0 ml with the mobile phase. Dilute 1.0 ml of the solution to 100.0 ml with the mobile phase.

Reference solution (b). Dilute 2.0 ml of the test solution to 50.0 ml with the mobile phase. Dilute 5.0 ml of this solution to 100.0 ml with the mobile phase.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm,

– *stationary phase*: *silica gel for chromatography R* (5 µm).

Mobile phase: *dilute sulphuric acid R, water R, acetonitrile R* (0.4:6.6:93 *V/V/V*).

Flow rate: 1 ml/min.

Detection: spectrophotometer at 230 nm.

Injection: 20 µl.

Run time: 3 times the retention time of cetirizine.

System suitability: reference solution (a):

– *resolution*: minimum 3 between the peaks due to cetirizine and impurity A,

– *symmetry factors*: maximum 2.0.

Limits:

- *impurities A, B, C, D, E, F*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent),
- *unspecified impurities*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent),
- *total*: not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent),
- *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.02 per cent).

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulphated ash (*2.4.14*): maximum 0.2 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.100 g in 70 ml of a mixture of 30 volumes of *water R* and 70 volumes of *acetone R*. Titrate with *0.1 M sodium hydroxide* to the second point of inflexion. Determine the end-point potentiometrically (*2.2.20*). Carry out a blank titration.

1 ml of *0.1 M sodium hydroxide* is equivalent to 15.39 mg of $C_{21}H_{27}Cl_3N_2O_3$.

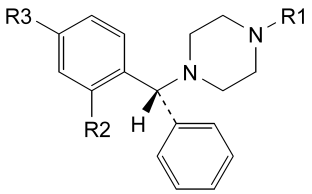
STORAGE

Protected from light.

IMPURITIES

Specified impurities: A, B, C, D, E, F.

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*): *G.*



and enantiomer

A. R1 = R2 = H, R3 = Cl: (*RS*)-1-[(4-chlorophenyl)phenylmethyl]piperazine,

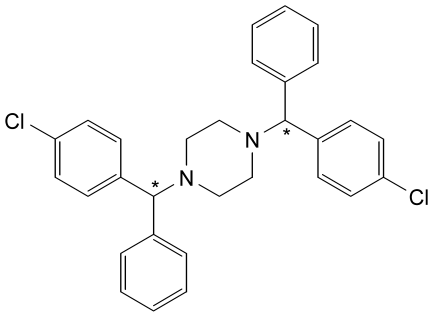
B. R1 = CH_2-CO_2H, R2 = H, R3 = Cl: (*RS*)-2-[4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl]acetic acid,

C. R1 = CH_2-CH_2-O-CH_2-CO_2H, R2 = Cl, R3 = H: (*RS*)-2-[2-[4-[(2-chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]acetic acid,

E. R1 = CH_2-[CH_2-O-CH_2]$_2$-CO_2H, R2 = H, R3 = Cl: (*RS*)-2-[2-[2-[4-[(4-chlorophenyl)phenylmethyl]piperazin-1-yl]ethoxy]ethoxy]acetic acid (ethoxycetirizine),

F. R1 = CH_2-CH_2-O-CH_2-CO_2H, R2 = R3 = H: [2-[4-(diphenylmethyl)piperazin-1-yl]ethoxy]acetic acid,

G. R1 = CH_2-CH_2-OH, R2 = H, R3 = Cl: 2-[4-[(*RS*)-(4-chlorophenyl)phenylmethyl]piperazin-1-yl]ethanol,



D. 1,4-bis[(4-chlorophenyl)phenylmethyl]piperazine.

01/2008:0702

CETOSTEARYL ALCOHOL

Alcohol cetylicus et stearylicus

DEFINITION

Mixture of solid aliphatic alcohols, mainly octadecan-1-ol (stearyl alcohol; $C_{18}H_{38}O$; M_r 270.5) and hexadecan-1-ol (cetyl alcohol; $C_{16}H_{34}O$; M_r 242.4), of animal or vegetable origin.

Content:

- *stearyl alcohol*: minimum 40.0 per cent,
- *sum of the contents of stearyl alcohol and cetyl alcohol*: minimum 90.0 per cent.

CHARACTERS

Appearance: white or pale yellow, wax-like mass, plates, flakes or granules.

Solubility: practically insoluble in water, soluble in ethanol (96 per cent) and in light petroleum. When melted, it is miscible with fatty oils, with liquid paraffin and with melted wool fat.

IDENTIFICATION

Examine the chromatograms obtained in the assay.

Results: the 2 principal peaks in the chromatogram obtained with the test solution are similar in retention time to the principal peaks in the chromatogram obtained with the reference solution.

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution B_6 (*2.2.2, Method II*).

Dissolve 0.50 g in 20 ml of boiling *ethanol (96 per cent) R*. Allow to cool.

Melting point (*2.2.14*): 49 °C to 56 °C.

Acid value (*2.5.1*): maximum 1.0.

Hydroxyl value (*2.5.3, Method A*): 208 to 228.

Iodine value (*2.5.4, Method A*): maximum 2.0.

Dissolve 2.00 g in *methylene chloride R* and dilute to 25 ml with the same solvent.

Saponification value (*2.5.6*): maximum 2.0.

ASSAY

Gas chromatography (*2.2.28*): use the normalisation procedure.

Test solution. Dissolve 0.100 g of the substance to be examined in *ethanol (96 per cent) R* and dilute to 10.0 ml with the same solvent.