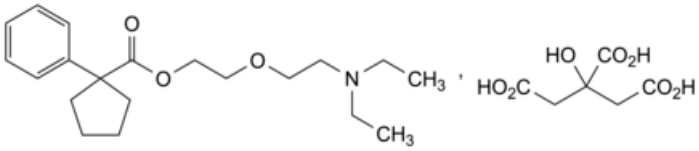
Edition: BP 2025 (Ph. Eur. 11.6 update)

Pentoxyverine Citrate

General Notices

(Pentoxyverine Hydrogen Citrate, Ph. Eur. monograph 1621)



$C_{26}H_{39}NO_{10}$ 525.6 *23142-01-0*

Action and use

Cough suppressant.

Ph Eur

DEFINITION

2-[2-(Diethylamino)ethoxy]ethyl 1-phenylcyclopentanecarboxylate dihydrogen 2-hydroxypropane-1,2,3-tricarboxylate.

Content

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

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Freely soluble in water, very soluble in glacial acetic acid, freely soluble in methanol, soluble in ethanol (96 per cent) and in methylene chloride.

mp

About 93 °C.

IDENTIFICATION

A. Infrared absorption spectrophotometry (2.2.24).

Comparison Ph. Eur. reference spectrum of pentoxyverine hydrogen citrate.

B. Dissolve 0.25 g in 5 mL of water R. The solution gives the reaction of citrates (2.3.1).

TESTS

Solution S

Dissolve 5.0 g in carbon dioxide-free water R and dilute to 50 mL with the same solvent.

Appearance of solution

Solution S is clear (2.2.1) and not more intensely coloured than reference solution Y_6 (2.2.2, Method II).

pH (2.2.3)

3.3 to 3.7 for solution S.

Related substances

Liquid chromatography (2.2.29).

Test solution Dissolve 25.0 mg of the substance to be examined in the mobile phase and dilute to 25.0 mL with the mobile phase.

Reference solution Introduce 5.0 mg of pentoxyverine impurity A CRS and 5.0 mg of pentoxyverine impurity B CRS in a conical flask, add 5.0 mL of the test solution and dilute to 100.0 mL with the mobile phase. Dilute 3.0 mL of the solution to 50.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.15 m, Ø = 3.9 mm,

— *stationary phase*: end-capped octylsilyl silica gel for chromatography R (5 µm) with a pore size of 10 nm and a carbon loading of 12 per cent,

— *temperature*: 50 °C.

Mobile phase Mix 35 volumes of acetonitrile R and 65 volumes of a 1.5 g/L solution of sodium heptanesulfonate R adjusted to pH 3.0 with dilute sulfuric acid R.

Flow rate 1.0 mL/min.

Detection Spectrophotometer at 205 nm.

Injection 20 µL.

Run time 3 times the retention time of pentoxyverine.

Relative retention With reference to pentoxyverine (retention time = about 6 min): impurity B = about 0.8; impurity A = about 1.5.

System suitability Reference solution:

— resolution: minimum of 5.0 between the peaks due to pentoxyverine and to impurity A,

— signal-to-noise ratio: minimum of 100 for the peak due to pentoxyverine,

— symmetry factor: maximum of 2.0 for the peak due to pentoxyverine.

Limits:

— *impurity A*: not more than the area of the corresponding peak in the chromatogram obtained with the reference solution (0.3 per cent),

— *impurity B*: not more than the area of the corresponding peak in the chromatogram obtained with the reference solution (0.3 per cent),

— *any other impurity*: not more than one-third of the area of the peak due to pentoxyverine in the chromatogram obtained with the reference solution (0.1 per cent),

— *total of any other impurity*: not more than the area of the peak due to pentoxyverine in the chromatogram obtained with the reference solution (0.3 per cent),

— *disregard limit*: 0.1 times the area of the peak due to pentoxyverine in the chromatogram obtained with the reference solution (0.03 per cent); disregard any peak with a retention time less than or equal to 2.5 min.

Loss on drying (*2.2.32*)

Maximum 0.5 per cent, determined on 1.000 g by drying *in vacuo* at 60 °C for 4 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

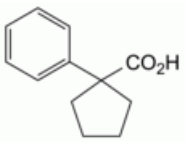
Dissolve 0.400 g in 70 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 52.56 mg of $C_{26}H_{39}NO_{10}$.

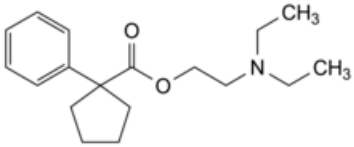
STORAGE

Protected from light.

IMPURITIES



A. 1-phenylcyclopentanecarboxylic acid,



B. 2-(diethylamino)ethyl 1-phenylcyclopentanecarboxylate (caramiphen).