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

Paracetamol Oral Solution

General Notices

Action and use

Analgesic; antipyretic.

DEFINITION

Paracetamol Oral Solution contains *Paracetamol* in a suitable flavoured vehicle.

The oral suspension complies with the requirements stated under Oral Liquids and with the following requirements.

Content of paracetamol, $C_8H_9NO_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Protect the solutions from light.

Solution A 15 volumes of *methanol* and 85 volumes of *water*.

(1) Shake a quantity of the oral solution containing 0.2 g of Paracetamol with solution A, add sufficient solution A to produce 25 mL, mix and filter (0.45 µm nylon filter is suitable), if necessary. Prepare immediately before use.
(2) Dilute 1 volume of solution (1) to 20 volumes with solution A and dilute 1 volume of the resulting solution to 50 volumes with solution A.
(3) 0.00008% w/v of *4-aminophenol* (paracetamol impurity K) in solution A. Prepare immediately before use.
(4) 0.02% w/v solution of *4'-chloroacetanilide* (paracetamol impurity J) in *methanol*, diluted in solution A to produce a solution containing 0.000008% w/v of *4'-chloroacetanilide*.
(5) Mix equal volumes of solution (2) and solution (3).

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped solid core octadecylsilyl silica gel for chromatography* (5 µm) (Halo C18 is suitable).
(b) Use gradient elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 30°.
(e) Use an autosampler at 5°.
(f) Use a detection wavelength of 254 nm.
(g) Inject 50 µL of each solution.

MOBILE PHASE

Mobile phase A Dissolve 1.7 g of *potassium dihydrogen phosphate* and 1.8 g of *dipotassium hydrogen phosphate* in *water* and dilute to 1000 mL with *water*.

Mobile phase B *Methanol*.

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
0-1.5	95	5	isocratic
1.5-14.5	95→90	5→10	linear gradient
14.5-29	90	10	isocratic
29-58	90→66	10→34	linear gradient
58-60	66	34	isocratic
60-65	66→95	34→5	linear gradient
65-70	95	5	re-equilibration

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (5), the *resolution* between the peaks due to paracetamol impurity K and paracetamol is at least 5.0.

CALCULATION OF IMPURITIES

For impurity K, use the concentration in solution (3).

For impurity J, use the concentration in solution (4).

For any other impurity, use the concentration of paracetamol in solution (2).

For the reporting threshold, use the concentration of paracetamol in solution (2).

Paracetamol retention time: about 4 minutes.

Relative retention: impurity K, about 0.4; impurity J, about 10.0.

LIMITS

— impurity K: not more than 100 ppm;

— impurity J: not more than 10 ppm;

— unspecified impurities: for each impurity, not more than 0.10%;

— total impurities: not more than 0.5%;

— reporting threshold: 0.05%.

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Protect solutions from light.

(1) Shake a quantity of the oral solution containing 0.5 g of Paracetamol with 80 mL of the mobile phase with the aid of ultrasound, add sufficient mobile phase to produce 100 mL, mix and filter, if necessary (0.45 µm nylon filter is suitable).

Dilute 1 volume of the resulting solution to 100 volumes with the mobile phase.
(2) 0.005% w/v of *paracetamol BPCRS* in the mobile phase.
(3) 0.002% w/v each of *4-aminophenol* and *paracetamol BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *base-deactivated octylsilyl silica gel for chromatography* (5 µm) (Zorbax Rx C8 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.5 mL per minute.
(d) Use a column temperature of 35°.
(e) Use a detection wavelength of 245 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

250 volumes of *methanol* containing 1.15 g of a 40% w/v solution of *tetrabutylammonium hydroxide*, 375 volumes of 0.05M *disodium hydrogen orthophosphate* and 375 volumes of 0.05M *sodium dihydrogen orthophosphate*.

SYSTEM SUITABILITY

The test is not valid unless in the chromatogram obtained with solution (3), the *resolution* between the two principal peaks is at least 4.0.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral solution, Appendix V G, and calculate the content of $C_8H_9NO_2$ in the oral solution from the chromatograms obtained, using the declared content of $C_8H_9NO_2$ in *paracetamol BPCRS*.

STORAGE

Paracetamol Oral Solution should be protected from light.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities J and K listed under Paracetamol.