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

Paracetamol Tablets

General Notices

Action and use

Analgesic; antipyretic.

DEFINITION

Paracetamol Tablets contain Paracetamol.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of paracetamol, $C_8H_9NO_2$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Extract a quantity of the powdered tablets containing 0.5 g of Paracetamol with 20 mL of *acetone*, filter, evaporate the filtrate to dryness and dry at 105°. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of paracetamol (*RS 258*).

TESTS

Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1. Protect the solutions from light.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of a phosphate buffer (pH 5.8), at a temperature of 37°, prepared in the following manner, as the medium. Mix 250 mL of *0.2M potassium dihydrogen phosphate* and 18 mL of *0.2M sodium hydroxide*, and dilute to 1000 mL with *water*.

PROCEDURE

(1) After 45 minutes withdraw a sample of the medium and filter (0.45 µm nylon filter is suitable). Dilute the filtrate, if necessary, with sufficient dissolution medium to produce a solution expected to contain about 0.005% w/v of Paracetamol.
(2) 0.005% w/v of *paracetamol BPCRS* in the dissolution medium.

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*.

DETERMINATION OF CONTENT

Calculate the total content of paracetamol, $C_8H_9NO_2$, from the chromatograms obtained, using the declared content of $C_8H_9NO_2$ in *paracetamol BPCRS*.

LIMITS

The amount of paracetamol released is not less than 75% (Q) of the stated amount.

Related substances

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

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

(1) Disperse a quantity of powdered tablets containing 0.2 g of Paracetamol in 20 mL of solution A with the aid of ultrasound, add sufficient solution A to produce 25 mL, mix and filter (0.45 µm nylon filter is suitable). 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

Time (Minutes)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comment
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

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D. Protect the solutions from light.

(1) Disperse a quantity of the powdered tablets containing 0.5 g of Paracetamol in 80 mL of the mobile phase with the aid of ultrasound, add sufficient mobile phase to produce 100 mL, mix, filter (0.45 µm nylon filter is suitable) and 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

The chromatographic conditions described under Dissolution may be used.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to 4-aminophenol and paracetamol is at least 4.0.

DETERMINATION OF CONTENT

Calculate the content of $C_8H_9NO_2$ in the tablets from the chromatograms obtained, using the declared content of $C_8H_9NO_2$ in *paracetamol BPCRS*.

STORAGE

Paracetamol Tablets should be protected from light.

IMPURITIES

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