

Paracetamol oral solution (Paracetamoli solutio peroralum)

2025-01

Other name. Acetaminophen oral solution.

Category. Non-opioid analgesic.

Storage. Paracetamol oral solution should be kept in a well-closed container having a child-resistant closure, protected from light.

Additional information. Strength in the current WHO Model list of essential medicines: 125 mg per 5 mL (25 mg per mL). Strength in the current WHO Model list of essential medicines for children: 125 mg per 5 mL (25 mg per mL).

Requirements

Complies with the monograph for "[Liquid preparations for oral use](#)".

Definition. Paracetamol oral solution is a solution of Paracetamol in a suitable vehicle, which may be flavoured. It contains not less than 90.0% and not more than 110.0% of the amount of paracetamol ($C_8H_9NO_2$) stated on the label.

Identity tests

A. Carry out test A.1 or, where UV detection is not available, test A.2.

A.1 Carry out the test as described under [1.14.1 Chromatography, Thin-layer chromatography](#), using silica gel R6 as the coating substance and a mixture of 50 volumes of acetone R, 50 volumes of toluene R and 1 volume of glacial acetic acid R as the mobile phase.

Apply separately to the plate 10 µl of each of the following two solutions. For solution (A) shake a volume of the oral solution containing 125 mg of Paracetamol with 25 mL of methanol R, dilute to 50 mL with the same solvent, filter, and use the filtrate. For solution (B) use 2.5 mg of paracetamol RS per mL of methanol R.

After removing the plate from the chromatographic chamber allow it to dry in a current of air.

Examine the chromatogram in ultraviolet light (254 nm).

The principal spot obtained with solution (A) corresponds in position, appearance and intensity to that obtained with solution (B).

A.2 Carry out the test as described under [1.14.1 Chromatography, Thin-layer chromatography](#), using the conditions described above under test A.1 but using silica gel R5 as the coating substance. After removing the plate from the chromatographic chamber allow it to dry in a current of air. Expose the plate to iodine vapours until spots appear and examine the chromatogram in daylight.

The principal spot obtained with solution (A) corresponds in position, appearance and intensity to that obtained with solution (B).

B. See the test described below under Assay. The retention time of the principal peak in the chromatogram obtained with solution (1) corresponds to that obtained with solution (2).

4-Aminophenol

Prepare fresh solutions, protect solutions from light and perform the test without delay. Carry out the test as described under [1.14.1 Chromatography, High-performance liquid chromatography](#), using the same chromatographic conditions as described under Assay but using 272 nm as the detection wavelength.

Prepare the following solutions. For solution (1) shake a quantity of the oral solution containing 125 mg of Paracetamol with about 15 mL of the solvent mixture. Dilute to 25 mL with the solvent mixture. Filter through a 0.45 µm filter, discarding the first few mL of the filtrate. For solution (2) dissolve 12.5 mg of 4-aminophenol R and 12.5 mg of paracetamol RS in about 20 mL of solvent mixture and dilute to 50 mL with the solvent mixture. Dilute 5 mL of this solution to 50 mL with the solvent mixture.

Inject separately 20 µl each of solutions (1) and (2) and record the chromatograms. (Depending on the formulation of the oral solution there may be late-eluting preservatives or other excipients (e.g. potassium sorbate, sodium benzoate, vanillin and methyl hydroxybenzoate) present that can interfere with subsequent chromatographic runs.)

In the chromatogram obtained with solution (2) the following peak is eluted at the following relative retention, with reference to paracetamol (retention time about 8.5 minutes): 4-aminophenol about 0.54. The test is not valid unless the resolution between the peaks corresponding to 4-aminophenol and paracetamol in the chromatogram obtained with solution (3) is at least 4.0.

In the chromatogram obtained with solution (1) the area of any peak corresponding to 4-aminophenol is not greater than the area of the corresponding peak in the chromatogram obtained with solution (2) (0.5%).

Assay

Carry out the test as described under [1.14.1 Chromatography, High-performance liquid chromatography](#), using a stainless steel column (25 cm x 4.6 mm), packed with octasilyl silica gel for chromatography (5 µm). Prepare a solvent mixture consisting of 0.4 volumes of formic acid (~1080 g/l) TS, 15 volumes of methanol R and 85 volumes of water R. As the mobile phase use a filtered and degassed solution of 0.01 M sodium butanesulfonate R in the above solvent mixture.

Operate with a flow rate of 1.0 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of 243 nm.

Prepare the following solutions. For solution (1) shake an accurately weighed quantity of the oral solution containing about 25 mg of Paracetamol with about 60 mL of the solvent mixture. Dilute to 100 mL with the solvent mixture. Dilute 10 mL of the resulting solution to 50 mL with the solvent mixture. Filter a portion of this solution through a 0.45 µm filter, discarding the first few mL of the filtrate. For solution (2) accurately weigh about 12.5 mg of paracetamol RS and dissolve in about 30 mL of solvent mixture. Dilute this solution to 50 mL with the solvent mixture. Dilute 10 mL of the resulting solution to 50 mL with the solvent mixture. For solution (3) dissolve 12.5 mg of 4-aminophenol R and 12.5 mg of paracetamol RS in about 20 mL of solvent mixture, and dilute to 50 mL with the solvent mixture. Dilute 5 mL of this solution to 50 mL with the solvent mixture.

Inject separately 20 µl each of solutions (1), (2) and (3) and record the chromatograms.

In the chromatogram obtained with solution (3) the following peak is eluted at the following relative retention, with reference to paracetamol (retention time about 8.5 minutes): 4-aminophenol about 0.54. The test is not valid unless the resolution between the peaks corresponding to 4-aminophenol and paracetamol in the chromatogram obtained with solution (3) is at least 4.0.

Measure the areas of the peak responses in the chromatograms obtained with solutions (1) and (2).

Determine the weight per mL (1.3.1) of the oral solution and calculate the content of paracetamol (C₈H₉NO₂), weight in volume, in the oral solution.