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Naproxen Oral Suspension

General Notices

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

DEFINITION

Naproxen Oral Suspension is a suspension of Naproxen in a suitable flavoured vehicle.

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

Content of naproxen, $C_{14}H_{14}O_3$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Filter a quantity of the oral suspension containing 0.1 g of Naproxen (Whatman 541 is suitable), wash the residue with two 5-mL aliquots of *water* and allow to dry. Shake the residue with 20 mL of *methanol*, filter the resulting solution through a 0.45-µm nylon filter and evaporate the filtrate to dryness. Dry the residue at 105° for 30 minutes. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of naproxen *(RS 244)*.

TESTS

Acidity

pH, 2.4 to 5.0, Appendix V L.

Dissolution

Carry out the test for dissolution described under *dissolution test for tablets and capsules*, Appendix XII B1. The solutions should be protected from light.

TEST CONDITIONS

(a) Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
(b) Use 900 mL of a phosphate buffer, prepared in the following manner, at a temperature of 37°, as the medium. Dissolve 2.62 g of *sodium dihydrogen orthophosphate monohydrate* and 11.50 g of *anhydrous disodium hydrogen orthophosphate* in sufficient *water* to produce 1 L, and adjusting the pH to 7.4 with either 0.1M *sodium hydroxide* or 0.1M *hydrochloric acid* if necessary.

PROCEDURE

(1) Shake the container containing the oral suspension being examined and accurately remove 5 mL. Introduce the dose to the medium in the dissolution vessel. After 15 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium if necessary, at the maximum at 332 nm, Appendix II B, using dissolution medium in the reference cell.
(2) Measure the *absorbance* of a suitable solution of *naproxen BPCRS* in the dissolution medium, using dissolution medium in the reference cell.

DETERMINATION OF CONTENT

Calculate the total content of naproxen, $C_{14}H_{14}O_3$, in the medium from the absorbances obtained and using the declared content of $C_{14}H_{14}O_3$ in *naproxen BPCRS*.

LIMITS

The amount of naproxen released is not less than 80% (Q) of the stated amount.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. The solutions should be freshly prepared and protected from light.

(1) Mix with the aid of ultrasound a quantity of the oral suspension containing 30 mg of Naproxen with 40 mL of the mobile phase, dilute to produce 50 mL and filter.
(2) Dilute 1 volume of solution (1) to 100 volumes with the mobile phase. Further dilute 1 volume of this solution to 10 volumes with the mobile phase.
(3) 0.03% w/v of *naproxen impurity standard BPCRS* in *acetonitrile*. Dilute 1 volume of this solution to 100 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (3 µm) (Nucleosil 120-3 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 50°.
(e) Use an autosampler temperature of 8°.
(f) Use a detection wavelength of 230 nm.
(g) Inject 20 µL of each solution.
(h) Allow the chromatography to proceed for 10 times the retention time of naproxen.

MOBILE PHASE

42 volumes of *acetonitrile* and 58 volumes of 0.01M *potassium dihydrogen orthophosphate* previously adjusted to pH 2.0 with *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions, the relative retentions with reference to naproxen (retention time about 2 minutes) are: impurity O, about 0.8; impurity K, about 0.9; impurity L, about 1.5 and impurity N, about 5.6.

SYSTEM SUITABILITY

The test is not valid unless:

in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity K and naproxen is at least 2.2;

in the chromatogram obtained with solution (2), the *signal-to-noise* ratio of the peak due to naproxen is at least 50.

LIMITS

In the chromatogram obtained with solution (1), identify any peaks corresponding to impurities L, N and O using the chromatogram obtained with solution (3), and multiply the areas of these peaks by the following correction factors: L, 3.5 and O, 1.8.

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than 1.6 times the area of the principal peak in the chromatogram obtained with solution (2) (0.16%);

the sum of the areas of any *secondary peaks* is not greater than 5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than half the area of the principal peak in the chromatogram obtained with solution (2) (0.05%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. The solutions should be protected from light.

(1) Mix with the aid of ultrasound a weighed quantity of the oral suspension containing 0.1 g of Naproxen with 80 mL of the mobile phase, dilute with sufficient mobile phase to produce 100 mL and filter. Dilute 1 volume of the filtrate to 100 volumes with the mobile phase.
(2) 0.001% w/v of *naproxen BPCRS* in the mobile phase.
(3) 0.03% w/v of *naproxen impurity standard BPCRS* in *acetonitrile*. Dilute 1 volume of this solution to 100 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances 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 impurity K and naproxen is at least 2.2.

DETERMINATION OF CONTENT

Determine the *weight per mL* of the oral suspension, Appendix V G, and calculate the content of $C_{14}H_{14}O_3$, weight in volume, using the declared content of $C_{14}H_{14}O_3$ in *naproxen BPCRS*.

STORAGE

Naproxen Oral Suspension should be protected from light.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Naproxen.