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

Caffeine Citrate Oral Solution

General Notices

Action and use

Respiratory and central nervous system stimulant.

DEFINITION

Caffeine Citrate Oral Solution is a solution of caffeine citrate, prepared by the interaction of Caffeine and Citric Acid Monohydrate, in a suitable aqueous vehicle. Sodium citrate may also be present.

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

Content of caffeine citrate, $C_8H_{10}N_4O_2,C_6H_8O_7$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using the following solution preparing a mixture containing 2 volumes of *methanol* and 3 volumes of *dichloromethane*.
(1) Dilute a volume of the oral solution containing the equivalent of 10 mg of caffeine to 100 mL.
(2) 0.01% w/v of *caffeine BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use as the coating *silica gel F_{254}*.
(b) Use the mobile phase as described below.
(c) Apply 10 µL of each solution.
(d) Develop the plate to 15 cm.
(e) After removal of the plate, dry in air and examine under *ultraviolet light* (254 nm).

MOBILE PHASE

1 volume of *concentrated ammonia*, 3 volumes of *acetone*, 3 volumes of *dichloromethane* and 4 volumes of *butan-1-ol*.

CONFIRMATION

The principal spot in the chromatogram obtained with solution (1) corresponds in position and colour to that in the chromatogram obtained with solution (2).

B. In the Assay, the chromatogram obtained with solution (1) shows a principal peak with the same retention time as the principal peak in the chromatogram obtained with solution (2).
C. Yields the reaction characteristic of *citrates*, Appendix VI.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in *water*.

(1) Dilute a volume of the oral solution containing the equivalent of 50 mg caffeine to 250 mL and filter through a 0.45-µm filter.
(2) Dilute 1 volume of solution (1) to 100 volumes and dilute 1 volume of the resulting solution to 5 volumes.
(3) 0.02% w/v each of *theobromine*, *1,7-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione* (impurity F), *theophylline BPCRS* and *caffeine BPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5µm) (Waters C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 275 nm.
(f) Inject 10 µL of each solution.

MOBILE PHASE

4 volumes of *tetrahydrofuran*, 5 volumes of *acetonitrile* and 191 volumes of 0.01M *anhydrous sodium acetate*, previously adjusted to pH 4.5 with *glacial acetic acid*.

SYSTEM SUITABILITY

The test is not valid unless, the chromatogram obtained with solution (3) has 4 distinct peaks and the *resolution* between the peaks due to theophylline and caffeine is at least 6.0.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.2%);

the sum of the areas of any *secondary peaks* is not greater than 2.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5%).

Disregard any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.1%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in *water*.

(1) Dilute a volume of the oral solution containing the equivalent of 50 mg caffeine to 250 mL and filter through a 0.45-µm filter.
(2) 0.02% w/v of *caffeine BPCRS*.
(3) 0.02% w/v each of *theobromine*, *1,7-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione*, *theophylline BPCRS* and *caffeine BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used.

SYSTEM SUITABILITY

The test is not valid unless, the chromatogram obtained with solution (3) has 4 distinct peaks and the *resolution* between the peaks due to theophylline and caffeine is at least 6.0.

DETERMINATION OF CONTENT

Calculate the content of $C_8H_{10}N_4O_2,C_6H_8O_7$ in the oral solution using the declared content of $C_8H_{10}N_4O_2$ in *caffeine BPCRS*.

Each mg of $C_8H_{10}N_4O_2$ is equivalent to 1.989 mg of $C_8H_{10}N_4O_2,C_6H_8O_7$

LABELLING

The quantity of active ingredient is stated in terms of the amount of caffeine citrate and the equivalent amount of caffeine.

IMPURITIES

The impurities limited by the requirements of this monograph include impurities A, B, C, D and F listed under Caffeine.