Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-Aug-2014
Document Type: USP Monographs
DocId: GUID-3F2BAB06-5F88-44C7-AD4A-7A730E39F950_1_en-US
DOI: https://doi.org/10.31003/USPNF_M13940_01_01
DOI Ref: 12qc2

Cefadroxil Capsules

DEFINITION
Cefadroxil Capsules contain the equivalent of NLT 90.0% and NMT 120.0% of the labeled amount of cefadroxil ($C_{16}H_{17}N_3O_5S$).

IDENTIFICATION
• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **Procedure**

Buffer: 6.8 g/L of monobasic potassium phosphate in water. Adjust with 10 N potassium hydroxide to a pH of 5.0.

Mobile phase: Acetonitrile and *Buffer* (40:960)

Standard solution: 1.06 mg/mL of USP Cefadroxil RS in *Buffer*. This solution contains the equivalent of 1 mg/mL of cefadroxil. Use this solution on the day prepared.

Sample solution: Remove the contents of NLT 10 Capsules as completely as possible, and weigh. Transfer a portion of the powder, nominally equivalent to 200 mg of cefadroxil, to a 200-mL volumetric flask. Dilute with *Buffer* to volume, and stir by mechanical means for 5 min. Use this solution on the day prepared.

Chromatographic system
(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 230 nm

Column: 4-mm × 25-cm; 5-µm packing L1

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.2

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of cefadroxil ($C_{16}H_{17}N_3O_5S$) in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times F \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Cefadroxil RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of cefadroxil in the *Sample solution* (mg/mL)

P = potency of cefadroxil in USP Cefadroxil RS (µg/mg)

F = conversion factor, 0.001 mg/µg

Acceptance criteria: 90.0%–120.0%

PERFORMANCE TESTS
• **Dissolution ⟨711⟩**

Medium: Water; 900 mL

Apparatus 1: 100 rpm

Time: 30 min

Standard solution: USP Cefadroxil RS in *Medium* at a known concentration similar to that in the *Sample solution*

Sample solution: Sample per *Dissolution ⟨711⟩*. Suitably dilute with *Medium*, if necessary, and filter.

Analysis: Determine the amount of cefadroxil ($C_{16}H_{17}N_3O_5S$) dissolved from UV absorbances at 263 nm of the *Sample solution* in comparison to the *Standard solution*.

Tolerances: NLT 80% (*Q*) of the labeled amount of cefadroxil ($C_{16}H_{17}N_3O_5S$) is dissolved.

- **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

- **Organic Impurities**

Solution A: 50 mg/mL of sodium hydroxide

Solution B: 4 g/L of monobasic sodium phosphate dihydrate in water, adjusted with *Solution A* to a pH of 5.2

Solution C: Acetonitrile and *Solution B* (1:1)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution B (%)	Solution C (%)
0	100	0
35	85	15
50	40	60
60	0	100
61	100	0
70	100	0

Diluent: 3.5 g/L of monobasic potassium phosphate and 4.6 g/L of dibasic sodium phosphate anhydrous

System suitability stock solution 1: 0.5 mg/mL of USP Cefadroxil Related Compound D RS in *Diluent*. Sonicate as needed to dissolve.

System suitability stock solution 2: 0.5 mg/mL of USP Cefadroxil Related Compound I RS in *Diluent*. Sonicate as needed to dissolve.

System suitability solution: 10 µg/mL of cefadroxil related compound D from *System suitability stock solution 1*, 10 µg/mL of cefadroxil related compound I from *System suitability stock solution 2*, and 1 mg/mL of USP Cefadroxil System Suitability Mixture RS in *Solution B*. Store refrigerated, and discard after 14 h.

Standard solution: 10 µg/mL of USP Cefadroxil RS in *Solution B*

Sample solution: Nominally, 1 mg/mL of cefadroxil in *Solution B* prepared as follows. Transfer the finely powdered contents of NLT 10 Capsules to a suitable volumetric flask, and add 50% of the final volume of *Solution B*. Sonicate with intermittent shaking. Cool to room temperature, dilute with *Solution B* to final volume, and mix. Centrifuge a portion of this solution, and filter the supernatant solution. Store refrigerated, and discard after 14 h.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1 mL/min

Injection volume: 20 µL

Autosampler temperature: 6°

System suitability

Samples: *System suitability solution* and *Standard solution*

[Note—The relative retention times for cefadroxil related compound D, cefadroxil related compound I, and cefadroxil are about 0.71, 0.80, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between cefadroxil related compound D and cefadroxil related compound I, *System suitability solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times P \times (F_1/F_2) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of cefadroxil from the *Standard solution*

C_S = concentration of USP Cefadroxil RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of cefadroxil in the *Sample solution* (mg/mL)

P = potency of cefadroxil in USP Cefadroxil RS (µg/mg)

F_1 = conversion factor, 0.001 mg/µg

F_2 = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. The reporting threshold is 0.05%.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Amoxicillin related compound I[a]	0.16	1.3	0.5
Cefadroxil related compound B[b]	0.52	0.63	0.5
Cefadroxil related compound D[c,d]	0.71	—	—
Diketopiperazine derivative[e]	0.89	1.3	0.5
Cefadroxil	1.0	—	—
N-Phenylglycyl delta-3 cefadroxil[f]	1.4	1.5	0.15
N-Phenylglycyl cefadroxil[g,d]	1.8	—	—
3-Hydroxy-4-methylthiophenone[h]	1.9	0.40	0.5
N-Ethoxycarbonyl 7-aminodesacetoxycephalosporanic acid[i,d]	2.2	—	—
O-Ethoxycarbonyl cefadroxil[j,d]	2.4	—	—
Any individual, unspecified impurity	—	—	0.2
Total impurities	—	—	2.0

[a] D-Hydroxyphenylglycine; (*R*)-2-Amino-2-(4-hydroxyphenyl)acetic acid.

[b] 7-Aminodesacetoxycephalosporanic acid; (6*R*,7*R*)-7-Amino-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

[c] L-Cefadroxil; (6*R*,7*R*)-7-[(*R*)-2-Amino-2-(4-hydroxyphenyl)acetamido]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

[d] Process impurities that are controlled in the drug substance are not to be reported, are not included in total impurities, and are listed here for information only.

[e] 3-(Aminomethylene)-6-(4-hydroxyphenyl)piperazine-2,5-dione.

[f] (6*R*,7*R*)-7-{(2*R*)-2-[2-Amino-2-(4-hydroxyphenyl)acetamido]-2-(4-hydroxyphenyl)acetamido}-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-3-ene-2-carboxylic acid.

[g] (6*R*,7*R*)-7-{(2*R*)-2-[2-Amino-2-(4-hydroxyphenyl)acetamido]-2-(4-hydroxyphenyl)acetamido}-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

[h] 3-Hydroxy-4-methylthiophen-2(5*H*)-one.

[i] (6*R*,7*R*)-7-(Ethoxycarbonylamino)-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

[j] (6*R*,7*R*)-7-((*R*)-2-Amino-2-{4-[(ethoxycarbonyl)oxy]phenyl}acetamido)-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

SPECIFIC TESTS

• **Water Determination,** *Method I* ⟨921⟩**:** NMT 7.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers.

• **Labeling:** Capsules prepared using the hemihydrate form of Cefadroxil are so labeled.

• **USP Reference Standards** ⟨11⟩

USP Cefadroxil RS

USP Cefadroxil Related Compound D RS

(6*R*,7*R*)-7-[(*S*)-2-Amino-2-(4-hydroxyphenyl)acetamido]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.

$C_{16}H_{17}N_3O_5S$ 363.39

USP Cefadroxil Related Compound I RS

(6*R*,7*R*)-7-[(*R*)-2-Amino-2-(4-hydroxyphenyl)acetamido]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-3-ene-2-carboxylic acid.

$C_{16}H_{17}N_3O_5S$ 363.39

USP Cefadroxil System Suitability Mixture RS

This is a mixture of cefadroxil and *O*-ethoxycarbonyl cefadroxil [(6*R*,7*R*)-7-((*R*)-2-Amino-2-{4-[(ethoxycarbonyl)oxy]phenyl}acetamido)-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid].

$C_{19}H_{21}N_3O_7S$ 435.45

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
CEFADROXIL CAPSULES	Documentary Standards Support	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. 45(6)

Current DocID: GUID-3F2BAB06-5F88-44C7-AD4A-7A730E39F950_1_en-US

DOI: https://doi.org/10.31003/USPNF_M13940_01_01

DOI ref: 12qc2