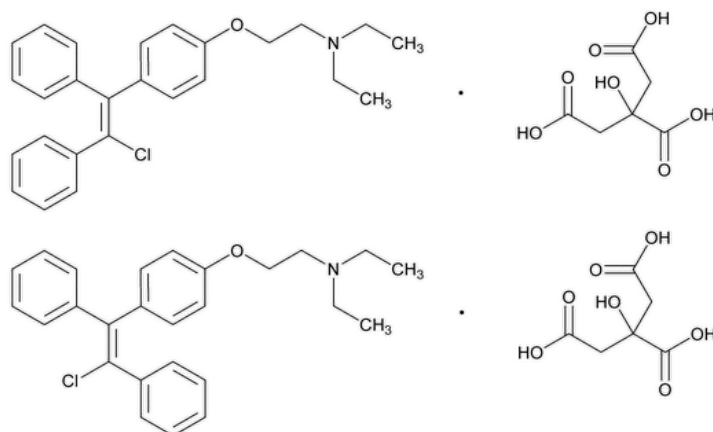


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Clomiphene Citrate



$C_{26}H_{28}ClNO \cdot C_6H_8O_7$ 598.08

Ethanamine, 2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethyl-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1);
 2-[p-(2-Chloro-1,2-diphenylvinyl)phenoxy]triethylamine citrate (1:1) CAS RN®: 50-41-9; UNII: 1B8447E7YI.

DEFINITION

Clomiphene Citrate contains NLT 98.0% and NMT 102.0% of a mixture of the (E)- and (Z)-geometric isomers of clomiphene citrate ($C_{26}H_{28}ClNO \cdot C_6H_8O_7$), calculated on the anhydrous basis. It contains NLT 30.0% and NMT 50.0% of the Z-isomer, [(Z)-2-[4-(2-chloro-1,2-diphenylethenyl)phenoxy]-N,N-diethylethanamine 2-hydroxy-1,2,3-propanetricarboxylate (1:1).

IDENTIFICATION

- **A. SPECTROSCOPIC IDENTIFICATION TESTS (197), Infrared Spectroscopy:** 197K

Change to read:

- **B. SPECTROSCOPIC IDENTIFICATION TESTS (197), Ultraviolet-Visible (ERR-1-Oct-2020) Spectroscopy:** 197U

Medium: 0.1 N hydrochloric acid

Sample solution: 20 µg/mL

Acceptance criteria: Meets the requirements

- **C. IDENTIFICATION TESTS—GENERAL, Citrate (191).**

ASSAY

PROCEDURE

Use low-actinic glassware for all solutions.

Mobile phase: Methanol, water, and triethylamine (55: 45: 0.3). Adjust with phosphoric acid to a pH of 2.5.

System suitability solution: 2 µg/mL of [USP Clomiphene Related Compound A RS](#) and 50 µg/mL of [USP Clomiphene Citrate RS](#), in *Mobile phase*

Standard solution: 50 µg/mL of [USP Clomiphene Citrate RS](#), in *Mobile phase*

Sample stock solution: 0.5 mg/mL of Clomiphene Citrate, in *Mobile phase*, filtered

Sample solution: 50 µg/mL of Clomiphene Citrate, in *Mobile phase*, from *Sample stock solution*

Chromatographic system

(See [Chromatography \(621\), System Suitability](#).)

Mode: LC

Detector: UV 233 nm

Column: 4.6-mm × 25-cm; packing L26

Flow rate: 1 mL/min

Injection volume: 50 µL

System suitability

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

[NOTE—The relative retention times for clomiphene related compound A, (Z)-isomer, and (E)-isomer are about 0.9, 1.0, and 1.2, respectively.]

Suitability requirements

Resolution: NLT 1.0 between clomiphene related compound A and (Z)-isomer; NLT 1.5 between (Z)-isomer and (E)-isomer, *System suitability solution*

Column efficiency: NLT 2000 theoretical plates for the (E)-isomer, *Standard solution*

Tailing factor: NMT 3.0 for the (E)-isomer, *Standard solution*

Relative standard deviation: NMT 2.0% for both (E)- and (Z)-isomers, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of clomiphene citrate ($C_{26}H_{28}ClNO \cdot C_6H_8O_7$) in the portion of Clomiphene Citrate taken:

$$\text{Result} = [(r_{UE} + r_{UZ}) / (r_{SE} + r_{SZ})] \times (C_S / C_U) \times 100$$

r_{UE} = peak response of the (E)-isomer from the *Sample solution*

r_{UZ} = peak response of the (Z)-isomer from the *Sample solution*

r_{SE} = peak response of the (E)-isomer from the *Standard solution*

r_{SZ} = peak response of the (Z)-isomer from the *Standard solution*

C_S = concentration of [USP Clomiphene Citrate RS](#) in the *Standard solution* (µg/mL)

C_U = concentration of Clomiphene Citrate in the *Sample solution* (µg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

OTHER COMPONENTS

• CONTENT OF (Z)-ISOMER

Mobile phase, System suitability solution, Standard solution, Sample solution, Chromatographic system, and System suitability: Proceed as directed in the Assay.

Analysis

Sample: *Sample solution*

Calculate the percentage of (Z)-isomer in the portion of Clomiphene Citrate taken:

$$\text{Result} = (r_Z / r_T) \times 100$$

r_Z = peak response of the (Z)-isomer from the *Sample solution*

r_T = sum of all the peak responses of the *Sample solution*

Acceptance criteria: 30.0%–50.0%

IMPURITIES

• ORGANIC IMPURITIES

Use low-actinic glassware for all solutions.

Buffer: Acetonitrile, diethylamine, and water (40: 0.8: 60). Adjust with phosphoric acid to a pH of 6.2.

Solution A: *Buffer* and water (90:10)

Solution B: *Buffer*

Mobile phase: See [Table 1](#).

Table 1