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Capecitabine Tablets

DEFINITION
Capecitabine Tablets contain NLT 93.0% and NMT 105.0% of the labeled amount of capecitabine ($C_{15}H_{22}FN_3O_6$).

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

Analytical wave number: 1500–1760 cm^{-1}

Sample: Grind 1 Tablet to a fine powder with a mortar and pestle. Mix 1 mg of this sample with 300 mg of potassium bromide.

• **B.** 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**

Diluent: Methanol, acetonitrile, and water (7:1:12)

Solution A: 0.1% mixture of glacial acetic acid in water

Solution B: Methanol, acetonitrile, and *Solution A* (7:1:12)

Solution C: Methanol, acetonitrile, and *Solution A* (16:1:3)

Mobile phase: See the gradient table below.

Time (min)	Solution B (%)	Solution C (%)
5	100	0
20	49	51
30	49	51
31	100	0
40	100	0
0	100	0

[Note—The following solutions may be sonicated as necessary.]

System suitability solution: Includes 0.6 µg/mL of USP Capecitabine RS, 0.6 µg/mL of USP Capecitabine Related Compound A RS, 0.6 µg/mL of USP Capecitabine Related Compound B RS, and 0.6 µg/mL of USP Capecitabine Related Compound C RS in *Diluent*

Standard solution: 0.6 mg/mL of USP Capecitabine RS in *Diluent*

Sample solution: Equivalent to 0.6 mg/mL of capecitabine, from powdered Tablets (NLT 20), in *Diluent*.[Note—Pass through a PVDF membrane filter of 0.45-µm pore size, and use the filtrate.]

Chromatographic system

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

Mode: LC

Detector: UV 250 nm

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

Column temperature: 40°

Autosampler temperature: 5°

Flow rate: 1 mL/min

Injection size: 10 µL

System suitability

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

[Note—For the purpose of peak identification, the approximate relative retention times are given in *Impurity Table 1*. The relative retention times are measured with respect to capecitabine.]

Suitability requirements

Resolution: NLT 1.0 between capecitabine related compound A and capecitabine related compound B, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{15}H_{22}FN_3O_6$ in the portion of Tablets taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

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

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

Acceptance criteria: 93.0%–105.0%

PERFORMANCE TESTS

• **Dissolution ⟨711⟩**

Medium: Water; 900 mL, degassed

Apparatus 2: 50 rpm

Time: 30 min

Standard solutions

For Tablets labeled to contain 150 mg: 17 mg of USP Capecitabine RS in 100 mL of *Medium*

For Tablets labeled to contain 500 mg: 28 mg of USP Capecitabine RS in 50 mL of *Medium*

Sample solution: Pass a portion of the solution under test through a fiberglass filter of 0.45-µm pore size.

Analysis: Determine the amount of $C_{15}H_{22}FN_3O_6$ dissolved by selecting a wavelength with appropriate sensitivity between 300 and 330 nm on portions of the *Sample solution*, suitably diluted with *Medium*, if necessary, in comparison with the appropriate *Standard solution*, using a 1-mm quartz cell. Calculate the percentage of $C_{15}H_{22}FN_3O_6$ dissolved in each Tablet:

$$\text{Result} = (A_U/A_S) \times C_S \times (V/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of capecitabine in the *Standard solution* (mg/mL)

V = volume of medium, 900 mL

L = Tablet label claim (mg)

Tolerances: NLT 80% (Q) of the labeled amount of $C_{15}H_{22}FN_3O_6$ is dissolved.

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

IMPURITIES

Organic Impurities

• **Procedure**

Diluent, Solution A, Solution B, Solution C, Mobile phase, System suitability solution, Standard solution, Sample solution, and

Chromatographic system: Proceed as directed in the *Assay*.

Analysis

Samples: *Standard solution* and *Sample solution*

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

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

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

r_S = peak response for capecitabine from the *Standard solution*

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

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

F = relative response factor for each impurity, from *Impurity Table 1*

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total degradation products: NMT 2.0%

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Capecitabine related compound A	0.18	1.05	1.0
Capecitabine related compound B	0.19	0.81	1.0
2',3'-Di-*O*-acetyl-5'-deoxy-5-fluorocytidine*	0.36	0.89	—
5'-Deoxy-5-fluoro-N4-(2-methyl-1-butyloxycarbonyl)cytidine + 5'-Deoxy-5-fluoro-N4-(3-methyl-1-butyloxycarbonyl)cytidine*	0.95	1.01	—
Capecitabine	1.00	1.00	—
[1-[5-Deoxy-3-*O*-(5-deoxy-β-D-ribofuranosyl)-β-D-ribofuranosyl]-5-fluoro-2-oxo-1,2-dihydropyrimidin-4-yl]-carbamic acid pentyl ester*	1.06	1.00	—
[1-[5-Deoxy-2-*O*-(5-deoxy-β-D-ribofuranosyl)-β-D-ribofuranosyl]-5-fluoro-2-oxo-1,2-dihydropyrimidin-4-yl]-carbamic acid pentyl ester*	1.09	1.00	—
Capecitabine related compound C	1.11	0.91	0.5
[1-[5-Deoxy-3-*O*-(5-deoxy-α-D-ribofuranosyl)-β-D-ribofuranosyl]-5-fluoro-2-oxo-1,2-dihydropyrimidin-4-yl]-carbamic acid pentyl ester*	1.20	1.00	—
2',3'-Di-*O*-acetyl-5'-deoxy-5-fluoro-N4-(pentyloxycarbonyl)cytidine*	1.37	0.85	—
Individual unspecified degradation product	—	1.00	0.1
The impurities marked with an "*" are process impurities and are not included in the total degradation products.			

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers. Store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩
  USP Capecitabine RS

USP Capecitabine Related Compound A RS
5'-Deoxy-5-fluorocytidine.
$C_9H_{12}FN_3O_4$ 245.21

USP Capecitabine Related Compound B RS
5'-Deoxy-5-fluorouridine.
$C_9H_{11}FN_2O_5$ 246.19

USP Capecitabine Related Compound C RS
2',3'-*O*-Carbonyl-5'-deoxy-5-fluoro-N^4-(pentyloxycarbonyl)cytidine.
$C_{16}H_{20}FN_3O_7$ 385.34

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

Topic/Question	Contact	Expert Committee
CAPECITABINE TABLETS	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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