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Mesalamine Extended-Release Capsules

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DEFINITION

Mesalamine Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of mesalamine (C₇H₇NO₃).

IDENTIFICATION

- A.**
Diluent: 0.01 N [hydrochloric acid](#) in [water](#)
Diluted standard solution: 0.025 mg/mL of [USP Mesalamine RS](#) in *Diluent*
Diluted sample solution: Nominally 0.025 mg/mL of [USP Mesalamine RS](#) in *Diluent* from the *Sample solution*, prepared as described in the Assay
Acceptance criteria: The UV spectrum of the major peak of the *Diluted sample solution* corresponds to that of the *Diluted standard solution*, as obtained in the Assay.
- 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

Change to read:

- PROCEDURE**
Buffer: 1.36 g/L of [monobasic potassium phosphate](#) in [water](#)
Solution A: 6.8 g/L of [monobasic potassium phosphate](#) in [water](#)
Solution B: [Acetonitrile](#) and *Buffer* (50:50)
Mobile phase: See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
10	100	0
20	60	40
22	60	40
22.1	100	0
30	100	0

- Diluent:** 0.01 N [hydrochloric acid](#) in [water](#)
Standard solution: 0.1 mg/mL of [USP Mesalamine RS](#) in *Diluent*
Sample stock solution: Nominally 1.0 mg/mL of mesalamine from Capsules prepared as follows. Transfer a portion of the contents of Capsules (NLT 20), nominally equivalent to 100 mg of mesalamine, to a suitable volumetric flask. Add 50% ▲to up to 80%▲ (RB 1-Jul-2024) of the flask volume of *Diluent*, and sonicate for ▲NLT▲ (RB 1-Jul-2024) 30 min. Dilute with *Diluent* to volume, and mix. Centrifuge the solution at 3000 rpm for 10 min.
Sample solution: Nominally 0.1 mg/mL of mesalamine in *Diluent*, from the *Sample stock solution*. Pass a portion of the solution through a suitable filter of 0.45-µm pore size.
Chromatographic system
(See [Chromatography \(621\)](#), *System Suitability*.)
Mode: LC

Detector: UV 230 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 25-cm; 5-μm packing [L1](#)

Temperatures

Autosampler: 5°

Column: 30°

Flow rate: 0.8 mL/min

Injection volume: 20 μL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 1.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of mesalamine ($C_7H_7NO_3$) in the portion of Capsules taken:

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

r_U = peak response of mesalamine from the *Sample solution*

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

C_S = concentration of [USP Mesalamine RS](#) in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

- [DISSOLUTION \(711\)](#).

Test 1

Buffer: 0.05 M pH 7.5 phosphate buffer prepared as follows. Dissolve 6.8 g of [monobasic potassium phosphate](#) and 1 g of [sodium hydroxide](#) in [water](#) to make 1000 mL of solution. Adjust with 10 N [sodium hydroxide](#) to a pH of 7.50 ± 0.05 .

Medium: *Buffer*; 900 mL

Apparatus 2: 100 rpm

Times: 1, 2, 4, and 8 h

Standard solution: A known concentration of [USP Mesalamine RS](#) in *Medium*

Sample solution: Filter portions of the solution under test suitably diluted with *Medium*, if necessary.

Analysis: Calculate the percentages of the labeled amount of mesalamine ($C_7H_7NO_3$) dissolved at the wavelength of maximum absorbance at about 330 nm by comparing the UV absorbances of the *Sample solution* with that of the *Standard solution*.

Tolerances: See [Table 2](#).

Table 2

Time (h)	Amount Dissolved (%)
1	5–25
2	30–50
4	60–90
8	NLT 85

The percentages of the labeled amount of mesalamine ($C_7H_7NO_3$) dissolved at the times specified conform to [Dissolution \(711\)](#),

[Acceptance Table 2](#).

Test 2: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 2*.

Acid stage

Medium: 0.1 N [hydrochloric acid](#); 750 mL, deaerated. [NOTE—After *Acid stage*, do not discard the solution. Retain the Capsules in proper order and proceed immediately as directed for *Buffer stage*.]

Apparatus 1: 100 rpm

Time: 2 h

Standard solution: 0.06 mg/mL of [USP Mesalamine RS](#) in *Medium*

Sample solution: Withdraw a portion of the solution under test and pass through a suitable filter of 0.45-μm pore size and discard the first few milliliters. Add the same volume of *Medium* to the dissolution vessel.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy \(857\)](#).)

Mode: UV

Analytical wavelength: 302 nm

Cell: 0.5 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of mesalamine ($C_7H_7NO_3$) dissolved:

$$\text{Result}_1 = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of [USP Mesalamine RS](#) in the *Standard solution* (mg/mL)

V = volume of *Medium*, 750 mL

L = label claim (mg/Capsule)

Tolerances: NMT 10%. The percentage of the labeled amount of mesalamine ($C_7H_7NO_3$) dissolved at the time specified conforms to

[Dissolution \(711\)](#), [Acceptance Table 3](#).

Buffer stage

Medium: After the *Acid stage*, immediately add 250 mL of 0.20 M sodium phosphate buffer solution [dissolve about 76 g of [sodium phosphate, tribasic](#) (dodecahydrate), in 1000 mL of [water](#); adjust, if necessary, with 10% (v/v) [phosphoric acid](#) or 2 N [sodium hydroxide](#) to a pH of 12.2] to the dissolution vessels containing the *Acid stage medium* (750 mL of 0.1 N hydrochloric acid). Adjust, if necessary, with 2 N [sodium hydroxide](#) or 2 N [hydrochloric acid](#) to a pH of 6.8; deaerated.

Apparatus 1: 100 rpm

Times: 0.5, 1, and 7 h

Solution A: Dissolve 3.4 g of [tetrabutylammonium hydrogen sulfate](#) and 1.4 g of [sodium acetate](#) (trihydrate) in 1000 mL of [water](#). Adjust with 1 N [sodium hydroxide](#) to a pH of 6.6. Add 200 mL of [acetonitrile](#).

Solution B: Dissolve 4.6 g of [tetrabutylammonium hydrogen sulfate](#) and 1.9 g of [sodium acetate](#) (trihydrate) in 1000 mL of [water](#). Adjust with 1 N [sodium hydroxide](#) to a pH of 6.6. Add 650 mL of [acetonitrile](#).

Mobile phase: *Solution A* and *Solution B* (90:10)

Standard solution: 0.06 mg/mL of [USP Mesalamine RS](#) in *Medium*

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-μm pore size and discard the first few milliliters. Add the same volume of *Medium* to the dissolution vessel. Dilute with *Medium*, if necessary, to obtain a solution with a similar concentration as the *Standard solution*.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

Column: 4.6-mm × 10-cm; 3-μm packing [L1](#)

Temperatures

Autosampler: 5°

Column: 25°

Flow rate: 1.0 mL/min

Injection volume: 10 μL

Run time: NLT 1.7 times the retention time of mesalamine

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_p) of mesalamine ($C_7H_7NO_3$) in the sample withdrawn from the vessel at each time point (t).

$$\text{Result}_i = (r_U/r_S) \times C_S \times D$$

r_U = peak response of mesalamine from the *Sample solution*

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

C_S = concentration of [USP Mesalamine RS](#) in the *Standard solution* (mg/mL)

D = dilution factor for the *Sample solution*

Calculate the percentage of the labeled amount of mesalamine ($C_7H_7NO_3$) dissolved at each time point (i):

$$\text{Result}_1 = C_1 \times V \times (1/L) \times 100$$

$$\text{Result}_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$\text{Result}_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

C_i = concentration of mesalamine in the portion of sample withdrawn at time point i (mg/mL)

V = volume of *Medium*, 1000 mL

L = label claim (mg/Capsule)

V_S = volume of the *Sample solution* withdrawn at each time point from the *Medium* (mL)

Tolerances: See [Table 3](#).

Table 3

Time Point (i)	Time (h)	Amount Dissolved (%)
1	0.5	18–43
2	1	35–55
3	7	NLT 80

The percentages of the labeled amount of mesalamine ($C_7H_7NO_3$) dissolved at the times specified conform to [Dissolution <711>](#), [Acceptance Table 2](#).

Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.

Acid stage

Medium: 0.1 N [hydrochloric acid](#); 750 mL

Apparatus 1: 100 rpm

Time: 2 h

Standard solution: 0.035 mg/mL of [USP Mesalamine RS](#) in *Medium*. Sonicate to dissolve if necessary.

Sample solution: At the end of the 2-h *Acid stage*, withdraw 13 mL of the solution under test and pass through a suitable filter of 0.45-μm pore size. Discard the first 5 mL of the filtrate.

Instrumental conditions

(See [Ultraviolet-Visible Spectroscopy <857>](#).)

Mode: UV

Analytical wavelength: 302 nm

Cell: 1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of mesalamine ($C_7H_7NO_3$) dissolved in the *Acid stage*:

$$\text{Result} = (A_U/A_S) \times C_S \times V \times (1/L) \times 100$$

A_U = absorbance of the *Sample solution*

A_S = absorbance of the *Standard solution*

C_S = concentration of [USP Mesalamine RS](#) in the *Standard solution* (mg/mL)