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Mesalamine Extended-Release Capsules

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click www.uspnf.com/rb-mesalamine-erc-20240628.

DEFINITION
Mesalamine Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of mesalamine ($C_7H_7NO_3$).

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_i) of mesalamine ($C_7H_7NO_3$) in the sample withdrawn from the vessel at each time point (i):

$$Result_i = (r_U/r_S) \times C_S \times D$$

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*):

$$Result_1 = C_1 \times V \times (1/L) \times 100$$

$$Result_2 = [(C_2 \times V) + (C_1 \times V_S)] \times (1/L) \times 100$$

$$Result_3 = \{(C_3 \times V) + [(C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

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*:

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

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)

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: pH 6.8 phosphate buffer (dissolve 6.8 g of potassium phosphate, monobasic in each liter of water; adjust with 1 N sodium hydroxide solution to a pH of 6.8); 1000 mL

Apparatus 1: 100 rpm

Times: 0.5, 2, and 7 h

Standard solution: 0.03 mg/mL of USP Mesalamine RS in *Medium*. Sonicate to dissolve if necessary. [NOTE—The *Standard solution* is stable for 20 h at room temperature.]

Sample solution: After the 2-h *Acid stage*, discard the *Acid stage medium* and carefully keep the remaining Capsule contents in the vessels. Add 1000 mL of *Buffer stage medium* into the vessels and continue with the *Buffer stage* conditions. At the specified time points, pass 13 mL of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first 5 mL of the filtrate. Dilute 2.0 mL of the filtrate with *Buffer stage medium* to 25.0 mL. Replace the 13 mL withdrawn at the 0.5 and 2 h time points with an equal volume of the *Buffer stage medium*. [NOTE—The *Sample solution* is stable for 11 h at room temperature.]

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: 331 nm

Cell: 1 cm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of mesalamine ($C_7H_7NO_3$) in the sample withdrawn from the vessel at each time point (i):

$$\text{Result}_i = (A_U/A_S) \times C_S \times D$$

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)

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 each time point (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 and replaced with the *Medium*, 13 mL

Tolerances: See *Table 4*.

Table 4

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	0.5	16–36
2	2	52–72
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 4: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.

Medium: 0.05 M pH 7.5 phosphate buffer (dissolve 6.8 g of potassium phosphate monobasic and 1 g of sodium hydroxide in 1000 mL of water; adjust with 10 N sodium hydroxide to a pH of 7.5); 900 mL, deaerated

Apparatus 2: 100 rpm

Times: 1, 2, 4, and 8 h

Standard solution: 0.033 mg/mL of USP Mesalamine RS in *Medium*. Sonicate to dissolve. [Note—The *Standard solution* is stable for 6 h at room temperature.]

Sample solution: At the specified time points, withdraw a known volume of the solution under test and replace with equal volume of fresh *Medium*. Pass the withdrawn solution through a suitable filter of 0.45-µm pore size, discarding the first 4 mL of the filtrate. Dilute with *Medium* to a concentration similar to that of the *Standard solution*. Pass through a suitable filter of 0.45-µm pore size, discarding the first 5 mL of the filtrate. [Note—The unfiltered *Sample solution* is stable for 16 h at room temperature. After filtration it is recommended to measure the *Sample solution* absorbance within 2 h.]

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

Mode: UV

Analytical wavelength: 330 nm

Blank: *Medium*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration (C_i) of mesalamine ($C_7H_7NO_3$) in the sample withdrawn from the vessel at each time point (*i*):

$$\text{Result}_i = (A_U/A_S) \times C_S \times D$$

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)

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*):

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

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

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

$$\text{Result}_4 = \{(C_4 \times V) + [(C_3 + C_2 + C_1) \times V_S]\} \times (1/L) \times 100$$

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

V = volume of *Medium*, 900 mL

L = label claim (mg/Capsule)

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

Tolerances: See *Table 5*.

Table 5

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	1	10–30
2	2	30–50
3	4	62–87
4	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 5: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 5*.

Acid stage medium: 0.1 N hydrochloric acid; 750 mL, deaerated.

After the *Acid stage*, do not discard the solution, retain the Capsules in proper order and proceed immediately as directed for the *Buffer stage*. The time between completion of acid stage dissolution and starting of buffer stage dissolution should be NMT 30 min.

Solution A: 0.20 M sodium phosphate buffer solution prepared as follows. Dissolve 76 g of sodium phosphate, tribasic in 1000 mL of water. Adjust with 10% (v/v) phosphoric acid or 2 N sodium hydroxide to a pH of 12.2.

Buffer stage medium: pH 6.8 phosphate buffer. (After the *Acid stage*, add 250 mL of *Solution A* to the dissolution vessels containing the *Acid stage medium*. Adjust with 2 N sodium hydroxide or 2 N hydrochloric acid to a pH of 6.8); 1000 mL, deaerated.

Apparatus 1: 100 rpm

Times

Acid stage: 2 h

Buffer stage: 0.5, 1, and 7 h. The time in the *Buffer stage medium* does not include the time in the *Acid stage medium*.

Acid stage standard solution: 0.05 mg/mL of USP Mesalamine RS in *Acid stage medium*. Sonicate to dissolve, if necessary. Allow to cool at room temperature. [NOTE—The *Acid stage standard solution* may be stable for 10 h at room temperature or in a refrigerator.]

Buffer stage standard solution: 0.375 mg/mL of USP Mesalamine RS in *Buffer stage medium*. Sonicate to dissolve, if necessary. Allow to cool at room temperature.

Acid stage sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained. Replace the portion withdrawn with the same volume of *Acid stage medium* in the dissolution vessel. [NOTE—The *Acid stage sample solution* may be stable for 20 h at room temperature or in a refrigerator.]

Buffer stage sample solution: At the specified time interval, pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding an appropriate volume of filtrate so that a consistent result can be obtained. Replace the portion withdrawn with the same volume of *Buffer stage medium* in the dissolution vessel.

Solution B: Dissolve 6.9 g of sodium phosphate, monobasic in 1000 mL of water. Adjust with 1 N sodium hydroxide to a pH of 6.2.

Mobile phase: Methanol and *Solution B* (5:95)

Chromatographic system

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

Mode: LC

Detector: UV 330 nm

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

Column temperature: 40°

Flow rate: 1.2 mL/min

Injection volume: 5 µL

Run time: NLT 1.8 times the retention time of mesalamine

System suitability

Samples: *Acid stage standard solution* and *Buffer stage standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for both *Acid stage standard solution* and *Buffer stage standard solution*

Relative standard deviation: NMT 2.0% for both *Acid stage standard solution* and *Buffer stage standard solution*

Analysis

Samples: *Acid stage standard solution*, *Buffer stage standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

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

$$\text{Result} = (r_U/r_S) \times C_S \times V_A \times (1/L) \times 100$$

r_U = peak response of mesalamine from the *Acid stage sample solution*

r_S = peak response of mesalamine from the *Acid stage standard solution*

C_S = concentration of USP Mesalamine RS in the *Acid stage standard solution* (mg/mL)

V_A = volume of *Acid stage medium*, 750 mL

L = label claim (mg/Capsule)

Calculate the concentration (C_i) of mesalamine ($C_7H_7NO_3$) in the sample withdrawn from the vessel at each time point (i) during the *Buffer stage*:

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

r_U = peak response of mesalamine from the *Buffer stage sample solution*

r_S = peak response of mesalamine from the *Buffer stage standard solution*

C_S = concentration of USP Mesalamine RS in the *Buffer stage standard solution* (mg/mL)

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

$$\text{Result}_1 = [C_1 \times V_B \times (1/L) \times 100] + (Q_A \times V_{SA}/V_A)$$

$$\text{Result}_2 = \{[(C_2 \times V_B) + (C_1 \times V_{SB})] \times (1/L) \times 100\} + (Q_A \times V_{SA}/V_A)$$

$$\text{Result}_3 = (\{(C_3 \times V_B) + [(C_2 + C_1) \times V_{SB}]\} \times (1/L) \times 100) + (Q_A \times V_{SA}/V_A)$$

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

V_B = volume of *Buffer stage medium*, 1000 mL

L = label claim (mg/Capsule)

Q_A = the percentage of the labeled amount of mesalamine dissolved in the *Acid stage*

V_{SA} = volume of the *Acid stage sample solution* withdrawn at the *Acid stage* and replaced with *Acid stage medium* (mL)

V_A = volume of the *Acid stage medium*, 750 mL

V_{SB} = volume of the *Buffer stage sample solution* withdrawn at each time point of the *Buffer stage* and replaced with *Buffer stage medium* (mL)

Tolerances

Acid stage: 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: See *Table 6*.

Table 6

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	0.5	15–35
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 6:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 6*.

Acid stage medium: 0.1 N hydrochloric acid; 750 mL, deaerated, if necessary

Buffer stage medium: pH 6.8 phosphate buffer. (Add 250 mL of 0.2 M potassium phosphate monobasic solution and 112 mL of 0.2 N sodium hydroxide. Dilute with water to 1000 mL. Adjust with 0.2 M potassium phosphate monobasic solution or 0.2 N sodium hydroxide to a pH of 6.8, if necessary.); 1000 mL, deaerated, if necessary.

Apparatus 1: 100 rpm

Times

Acid stage: 2 h

Buffer stage: 0.5, 1, and 7 h. The time in the *Buffer stage medium* does not include the time in the *Acid stage medium*.

Diluent: Acetonitrile, methanol, and water (13:8:79). Adjust with phosphoric acid to a pH of 1.5.

Solution A: Dissolve 1.36 g of potassium phosphate monobasic and 2.2 g of octanesulfonic acid sodium salt in 890 mL of water. Adjust with phosphoric acid to a pH of 2.2.

Mobile phase: Acetonitrile, methanol, and *Solution A* (13:8:89)

Acid stage standard stock solution: 0.4 mg/mL of USP Mesalamine RS in *Diluent*. Sonicate to dissolve, if necessary.

Acid stage standard solution: 0.032 mg/mL of USP Mesalamine RS prepared as follows. Transfer a suitable volume of *Acid stage standard stock solution* to an appropriate volumetric flask and add 6% of the flask volume of *Acid stage medium*. Dilute with *Diluent* to volume.

Buffer stage standard stock solution: 0.4 mg/mL of USP Mesalamine RS in *Diluent*. Sonicate to dissolve, if necessary.

Buffer stage standard solution: 0.032 mg/mL of USP Mesalamine RS prepared as follows. Transfer a suitable volume of *Buffer stage standard stock solution* to an appropriate volumetric flask and add 8% of the flask volume of *Buffer stage medium*. Dilute with *Diluent* to volume.

Acid stage sample solution: Pass a portion of the solution under test through a suitable filter, discarding an appropriate volume of filtrate so that a consistent result can be obtained. Dilute 3 mL of the filtrate with *Diluent* to 50 mL.

Buffer stage sample solution: After the *Acid stage*, discard the *Acid stage medium* and carefully keep the remaining Capsule contents in the vessels. Add 1000 mL of *Buffer stage medium* into the vessels and continue with the *Buffer stage* conditions. At the specified time interval, pass a portion of the solution under test through a suitable filter, discarding an appropriate volume of filtrate so that a consistent result can be obtained. Dilute 4 mL of the filtrate with *Diluent* to 50 mL. Replace the portion withdrawn with the same volume of *Buffer stage medium* in the dissolution vessel.

Chromatographic system

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

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Column temperature: 60°

Flow rate: 1.2 mL/min

Injection volume: 20 µL

Run time: NLT 1.7 times the retention time of mesalamine

System suitability

Samples: *Acid stage standard solution* and *Buffer stage standard solution*

Suitability requirements

Tailing factor: NMT 2.0 for both *Acid stage standard solution* and *Buffer stage standard solution*

Relative standard deviation: NMT 2.0% for both *Acid stage standard solution* and *Buffer stage standard solution*

Analysis

Samples: *Acid stage standard solution*, *Buffer stage standard solution*, *Acid stage sample solution*, and *Buffer stage sample solution*

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

$$\text{Result} = (r_U/r_S) \times C_S \times V_A \times D \times (1/L) \times 100$$

r_U = peak response of mesalamine from the *Acid stage sample solution*

r_S = peak response of mesalamine from the *Acid stage standard solution*

C_S = concentration of USP Mesalamine RS in the *Acid stage standard solution* (mg/mL)

V_A = volume of *Acid stage medium*, 750 mL

D = dilution factor of the *Acid stage sample solution*

L = label claim (mg/Capsule)

Calculate the concentration (C_i) of mesalamine ($C_7H_7NO_3$) in the sample withdrawn from the vessel at each time point (i) during the *Buffer stage*:

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

r_U = peak response of mesalamine from the *Buffer stage sample solution*

r_S = peak response of mesalamine from the *Buffer stage standard solution*

C_S = concentration of USP Mesalamine RS in the *Buffer stage standard solution* (mg/mL)

D = dilution factor of the *Buffer stage sample solution*

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

$$\text{Result}_1 = [C_1 \times V_B \times (1/L) \times 100] + Q_A$$

$$\text{Result}_2 = \{[(C_2 \times V_B) + (C_1 \times V_{SB})] \times (1/L) \times 100\} + Q_A$$

$$\text{Result}_3 = (\{(C_3 \times V_B) + [(C_2 + C_1) \times V_{SB}]\} \times (1/L) \times 100) + Q_A$$

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

V_B = volume of *Buffer stage medium*, 1000 mL

L = label claim (mg/Capsule)

Q_A = the percentage of the labeled amount of mesalamine dissolved in the *Acid stage*

V_{S_B} = volume of the *Buffer stage sample solution* withdrawn at each time point of the *Buffer stage* and replaced with *Buffer stage medium* (mL)

Tolerances

Acid stage: 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: See *Table 7*.

Table 7

Time Point (*i*)	Time (h)	Amount Dissolved (%)
1	0.5	7–27
2	1	46–66
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*.▲ (RB 1-Jul-2024)

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

IMPURITIES

Change to read:

• **Organic Impurities**

Buffer, Solution A, Solution B, Diluent, and **Chromatographic system:** Proceed as directed in the *Assay*.

Mobile phase: See ▲*Table 8*.

Table 8▲ (RB 1-Jul-2024)

Time (min)	Solution A (%)	Solution B (%)
0	100	0
10	100	0
40	30	70
45	30	70
46	100	0
55	100	0

Sensitivity solution: 0.5 µg/mL of USP Mesalamine RS in *Diluent*

Standard solution: 0.001 mg/mL of USP Mesalamine RS in *Diluent*

Sample 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 25 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. Pass a portion of the solution through a suitable filter of 0.45-µm pore size.

System suitability

Samples: *Sensitivity solution* and *Standard solution*

Suitability requirements

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

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of any unspecified degradation product in the portion of Capsules taken:

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

r_U = peak response of any unspecified degradation product 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: The reporting threshold is 0.05%.

Any unspecified degradation product: NMT 0.13%

Total degradation products: NMT 0.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩
  USP Mesalamine RS

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

Topic/Question	Contact	Expert Committee
MESALAMINE EXTENDED-RELEASE CAPSULES	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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