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# Mesalamine Delayed-Release Tablets

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

**IDENTIFICATION**

***Change to read:***

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** ▲197A or▲ (USP 1-Dec-2024) 197K

  **Sample:** To about 50 mL of water add a quantity of finely powdered Tablets, nominally equivalent to about 800 mg of mesalamine. Boil the mixture for about 5 min, with constant stirring. Filter the hot solution, and allow the filtrate to cool. Collect the precipitated crystals, and dry at about 110°.

  **Acceptance criteria:** Meet the requirements

- **B.** The retention time of the mesalamine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

**ASSAY**

***Change to read:***

- **Procedure**

  ▲**Buffer:** Dissolve 1.8 g of monobasic potassium phosphate and 4.7 g of sodium 1-octanesulfonate in 1 L of water. Adjust with phosphoric acid to a pH of 2.1.

  **Mobile phase:** Methanol and *Buffer* (25:75)

  **Standard solution:** 0.2 mg/mL of USP Mesalamine RS in 0.01 N hydrochloric acid

  **Sample stock solution:** Nominally 0.8 mg/mL of mesalamine from Tablets prepared as follows. Finely powder Tablets (NLT 10). Transfer a portion nominally equivalent to about 400 mg of mesalamine to a 500-mL volumetric flask. Add 50 mL of 0.5 N hydrochloric acid, and sonicate for 15 min. Add 350 mL of water and stir vigorously for NLT 60 min. Dilute with water to volume, and mix.

  **Sample solution:** Nominally 0.2 mg/mL of mesalamine in water, from *Sample stock solution*. Pass a portion of the solution through a suitable filter of 0.45-µm or finer pore size.

  **Chromatographic system**

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

  **Mode:** LC

  **Detector:** UV 220 nm

  **Column:** 4.6-mm × 25-cm; 5-µm packing L7

  **Column temperature:** 30°

  **Flow rate:** 1.5 mL/min

  **Injection volume:** 10 µL

  **Run time:** NLT 1.3 times the retention time of mesalamine

  **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 Tablets 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)

▲ (USP 1-Dec-2024)

**Acceptance criteria:** 90.0%–110.0%

**PERFORMANCE TESTS**

• **Dissolution** ⟨711⟩

**Test 1**

**Solution A:** Transfer about 43.35 g of monobasic potassium phosphate and 1.65 g of sodium hydroxide to a 2-L volumetric flask. Dissolve in and dilute with water to volume, and mix. Adjust with 1 N sodium hydroxide or phosphoric acid to a pH of 6.0, and mix.

**Solution B:** Transfer 133.6 g of sodium hydroxide to a 2-L volumetric flask, dissolve in and dilute with water to volume, and mix.

**Medium**

**Acid stage:** 500 mL of 0.1 N hydrochloric acid

**Buffer stages:** 900 mL of *Solution A*

**Apparatus 2**

**Acid stage:** 100 rpm

**Buffer stage 1:** 100 rpm

**Buffer stage 2:** 50 rpm

**Times**

**Acid stage:** 2 h

**Buffer stage 1:** 1 h

**Buffer stage 2:** 90 min

**Acid stage:** After 2 h of operation, withdraw an aliquot of the fluid, discard the remaining solution, and retain the Tablets in proper order so that each will be returned later to its respective vessel. Blot the Tablets with a paper towel to dry, and proceed immediately as directed in *Buffer stage 1*.

**Standard solution:** A known concentration of USP Mesalamine RS in *Medium*, equivalent to about 1% of the labeled amount of mesalamine ($C_7H_7NO_3$)

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

**Instrumental conditions**

**Mode:** UV

**Analytical wavelength:** 302 nm (maximum absorbance)

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

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

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

$A_U$ = 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)

$V$ = volume of *Medium*, 500 mL

$L$ = label claim of mesalamine (mg/Tablet)

**Tolerances:** See *Table 1*. Continue testing through all levels unless the results conform at an earlier level.

**Buffer stage 1**

[Note—Use *Solution A* that has been equilibrated to a temperature of 37 ± 0.5°.]

Transfer *Solution A* to each of the dissolution vessels, and place each Tablet from the *Acid stage* into its respective vessel. After 1 h, remove a 50-mL aliquot, and proceed immediately as directed in *Buffer stage 2*.

**Standard solution:** A known concentration of USP Mesalamine RS in *Medium*, equivalent to about 1% of the labeled amount of mesalamine ($C_7H_7NO_3$)

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

**Instrumental conditions**

**Mode:** UV

**Analytical wavelength:** 330 nm (maximum absorbance)

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

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

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

$A_U$ = 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)

$V$ = volume of *Medium*, 900 mL

$L$ = label claim of mesalamine (mg/Tablet)

**Tolerances:** See *Table 1*. Continue testing through all levels unless the results conform at an earlier level.

**Table 1**

| Level | Number Tested | Acceptance Criteria |
|---|---|---|
| $L_1$ | 6 | No individual value exceeds 1% dissolved. |
| $L_2$ | 6 | Average of the 12 units ($L_1 + L_2$) is NMT 1% dissolved, and no individual unit is >10% dissolved. |
| $L_3$ | 12 | Average of the 24 units ($L_1 + L_2 + L_3$) is NMT 1% dissolved, and NMT 1 individual unit is >10% dissolved. |

**Buffer stage 2:** Add 50 mL of *Solution B* to each dissolution vessel to adjust to a pH of 7.2, and continue the run.

**Standard solution:** A known concentration of USP Mesalamine RS in *Medium*

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

**Instrumental conditions**

**Mode:** UV

**Analytical wavelength:** 332 nm (maximum absorbance)

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

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

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

$A_U$ = 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)

$V$ = volume of *Medium*, 900 mL

$L$ = label claim of mesalamine (mg/Tablet)

**Tolerances:** NLT 80% ($Q$) of the labeled amount of mesalamine ($C_7H_7NO_3$) is dissolved. The requirements are met if the quantities dissolved from the product conform to *Dissolution ⟨711⟩*, *Acceptance Table 4*. Continue testing through all levels unless the results conform at an earlier level.

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

**Solution A:** pH 6.4 phosphate buffer (21.7 g/L of monobasic potassium phosphate and 0.8 g/L of sodium hydroxide in water, adjusted with 5 N sodium hydroxide or phosphoric acid to a pH of 6.4)

**Solution B:** 3.3 N sodium hydroxide (136 g/L of sodium hydroxide in water)

**Medium**

**Acid stage:** 750 mL of 0.1 N hydrochloric acid

**Buffer stage 1:** 950 mL of *Solution A*

**Buffer stage 2:** 960 mL of pH 7.2 phosphate buffer

**Apparatus 2:** 100 rpm

**Times**

**Acid stage:** 2 h

**Buffer stage 1:** 1 h

**Buffer stage 2:** 1, 2, and 6 h

**Acid stage**

After 2 h of operation, withdraw a portion of the solution under test, discard the remaining solution, and retain the Tablets in proper order so that each will be returned later to its respective vessel. Blot the Tablets with a paper towel to dry and proceed immediately as directed in *Buffer stage 1*.

**Standard solution:** 0.016 mg/mL of USP Mesalamine RS in *Medium*. Sonicate to dissolve.

**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.

**Instrumental conditions**

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

**Mode:** UV

**Analytical wavelength:** 302 nm

**Blank:** *Medium*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

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

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

$A_U$ = 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 of mesalamine (mg/Tablet)

**Tolerances:** NMT 1% of the labeled amount of mesalamine ($C_7H_7NO_3$) is dissolved.

**Buffer stage 1**

[Note—Use *Solution A* that has been equilibrated to a temperature of 37 ± 0.5°.]

Transfer *Solution A* to each of the dissolution vessels, and place each Tablet from the *Acid stage* into its respective vessel. After 1 h, withdraw a 10-mL aliquot and proceed immediately as directed in *Buffer stage 2*.

**Standard solution:** 0.0125 mg/mL of USP Mesalamine RS in *Medium*. Sonicate to dissolve.

**Sample solution:** Pass a portion of the withdrawn solution under test through a suitable filter of 0.45-µm pore size and discard the first few milliliters.

**Instrumental conditions**

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

**Mode:** UV

**Analytical wavelength:** 330 nm

**Blank:** *Medium*

**Analysis:** Proceed as directed in the *Analysis* at *Acid stage*, using the *Medium* for *Buffer stage 1*.

**Tolerances:** NMT 1% of the labeled amount of mesalamine ($C_7H_7NO_3$) is dissolved.

**Buffer stage 2**

To adjust the pH of 940 mL of *Solution A* to a pH of 7.2, transfer 20 mL of *Solution B* into each dissolution vessel from *Buffer stage 1* and start the dissolution immediately.

At the end of the specified time point, withdraw 10 mL of the solution under test from each dissolution vessel and replace with 10 mL of *Medium* for *Buffer stage 2*.

**Standard solution:** 0.0315 mg/mL of USP Mesalamine RS in *Medium*. Sonicate to dissolve.

**Sample solution:** Dilute 2.5 mL of the withdrawn solution under test with *Medium* to 100 mL. Pass through a suitable filter of 0.45-µm pore size and discard the first few milliliters.

**Instrumental conditions**

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

**Mode:** UV

**Analytical wavelength:** 332 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 ($i$):

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

$A_U$ = 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*, 40

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 the *Medium*, 960 mL

$L$ = label claim (mg/Tablet)

$V_S$ = volume of the solution under test withdrawn at each time point (*i*) during *Buffer stage 2*, 10 mL

**Tolerances:** See *Table 2*.

**Table 2**

| Time Point (*i*) | Time (h) | Amount Dissolved (%) |
|---|---|---|
| 1 | 1 | NMT 35 |
| 2 | 2 | 35–60 |
| 3 | 6 | NLT 80 |

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

**Solution A:** pH 6.4 phosphate buffer [20.4 g/L of potassium phosphate, monobasic and 1.6 g/L of sodium hydroxide in water, adjusted with 1 N (or 5 N) sodium hydroxide or phosphoric acid to a pH of 6.4]

**Solution B:** pH 7.2 phosphate buffer [20.4 g/L of potassium phosphate, monobasic and 4.2 g/L of sodium hydroxide in water, adjusted with 1 N (or 5 N) sodium hydroxide or phosphoric acid to a pH of 7.2]

**Medium**

**Acid stage:** 0.1 N hydrochloric acid, 750 mL

**Buffer stage 1:** *Solution A*, 950 mL

**Buffer stage 2:** *Solution B*, 960 mL

**Apparatus 2**

**Acid stage:** 100 rpm

**Buffer stage 1:** 100 rpm

**Buffer stage 2:** 100 rpm

**Times**

**Acid stage:** 2 h

**Buffer stage 1:** 1 h

**Buffer stage 2:** 0.5 h and 1.5 h

**Buffer:** 5 g/L of potassium phosphate, monobasic in water, adjusted with phosphoric acid to a pH of 2.0 ± 0.05

**Mobile phase:** Acetonitrile and *Buffer* (20:80)

**Diluent:** *Solution B* and water (33:67)

**Standard solution:** 1.25 mg/mL of USP Mesalamine RS in *Diluent*. Sonicate to dissolve.

**Sample solutions**

**Acid stage:** Place 1 Tablet in each vessel containing *Medium, Acid stage*. At the specified *Times*, withdraw a portion of the solution under test using a suitable filter of 10-µm pore size. Centrifuge if necessary. Remove the Tablets from solution, dry the Tablets with a paper towel, and retain in the proper order. Proceed as directed in *Buffer stage 1*.

**Buffer stage 1:** Transfer each Tablet from *Acid stage* into the respective vessel containing *Medium, Buffer stage 1*. At the specified *Times*, withdraw a portion of the solution under test using a suitable filter of 10-µm pore size. Centrifuge if necessary. Remove the Tablets from solution, dry the Tablets with a paper towel, and retain in the proper order. Proceed as directed in *Buffer stage 2*.

**Buffer stage 2:** Transfer each Tablet from *Buffer stage 1* into the respective vessel containing *Medium, Buffer stage 2*. At the specified *Times*, withdraw a portion of the solution under test using a suitable filter of 10-µm pore size. Centrifuge if necessary.

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 330 nm

**Column:** 4.6-mm × 15-cm; 5-µm packing L9

**Column temperature:** 30°

**Flow rate:** 1.2 mL/min

**Injection volume:** 5 µL for *Acid stage* and *Buffer stage 1*; 2 µL for *Buffer stage 2*

**Run time:** NLT 2.5 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**

**Acid stage**

**Samples:** *Standard solution* and *Sample solution*

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

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

$r_U$ = 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)

$V$ = volume of *Medium*, 750 mL

$L$ = label claim (mg/Tablet)

**Buffer stage 1:** Proceed as directed for the *Acid stage* except the volume of *Medium* is 950 mL.

**Buffer stage 2**

**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 ($i$) as shown in *Table 4*:

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

$r_U$ = 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)

Calculate the percentage of the labeled amount of mesalamine ($C_7H_7NO_3$) dissolved at each time point ($i$) as shown in *Table 4*:

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

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

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

$V$ = volume of *Medium*, 960 mL

$L$ = label claim (mg/Tablet)

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

**Tolerances**

**Acid stage:** See *Table 3*.

**Buffer stage 1:** See *Table 3*.

**Table 3**

| Level | Number Tested | Acceptance Criteria |
|---|---|---|
| $L_1$ | 6 | No individual value exceeds 1% dissolved. |
| $L_2$ | 6 | Average of the 12 units ($L_1 + L_2$) is NMT 1% dissolved, and no individual unit is >10% dissolved. |
| $L_3$ | 12 | Average of the 24 units ($L_1 + L_2 + L_3$) is NMT 1% dissolved, and NMT 1 individual unit is >10% dissolved. |

**Buffer stage 2:** See *Table 4*.

**Table 4**

| Level | Number Tested | Acceptance Criteria | |
|---|---|---|---|
| | | Time Point 1 (0.5 h) | Time Point 2 (1.5 h) |
| $L_1$ | 6 | No individual value exceeds 65% dissolved. | Each unit is NLT 85% dissolved. |
| $L_2$ | 6 | Average of the 12 units ($L_1 + L_2$) is NMT 65% dissolved, and no individual unit is >75% dissolved. | Average of the 12 units ($L_1 + L_2$) is NLT 85% dissolved, and no unit is <75% dissolved. |
| $L_3$ | 12 | Average of the 24 units ($L_1 + L_2 + L_3$) is NMT 65% dissolved, NMT 2 units are >75%, and no unit is >85% dissolved. | Average of the 24 units ($L_1 + L_2 + L_3$) is NLT 85% dissolved, NMT 2 units are <75%, and no unit is <65% dissolved. |

**Test 4:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 4*.

**Solution A:** 0.2 M phosphate buffer (76.0 g/L of sodium phosphate, tribasic, dodecahydrate in water)

**Medium**

**Acid stage:** 0.1 N hydrochloric acid, 750 mL

**Buffer stage 1:** pH 6.4 phosphate buffer (after *Acid stage*, adjust with the addition of 200 mL of *Solution A* to the *Medium, Acid stage* to a pH of 6.4), 950 mL

**Buffer stage 2:** pH 7.2 phosphate buffer (after *Buffer stage 1*, adjust with the addition of about 10 mL of 2 M sodium hydroxide solution to the *Medium, Buffer stage 1* to a pH of 7.2), 960 mL

**Apparatus 2:** 100 rpm

**Times**

**Acid stage:** 2 h

**Buffer stage 1:** 1 h

**Buffer stage 2:** 1, 2, and 6 h

**Acid stage**

**Standard solution:** 0.016 mg/mL of USP Mesalamine RS in *Medium*. Sonicate to dissolve, if necessary.

**Sample solution:** At the specified *Times*, withdraw about 10 mL of the solution under test, pass through a suitable filter of 0.45-µm pore size, and collect the filtrate by discarding the first few milliliters. Replace with about 10 mL of *Medium*.

**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:

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

$A_U$ = 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)

$V$ = volume of *Medium*, 750 mL

$L$ = label claim of mesalamine (mg/Tablet)

**Tolerances:** NMT 1% of the labeled amount of mesalamine ($C_7H_7NO_3$) is dissolved.

**Buffer stage 1**

**Standard solution:** 0.012 mg/mL of USP Mesalamine RS in *Medium*. Sonicate to dissolve, if necessary.

**Sample solution:** At the specified *Times*, withdraw about 10 mL of the solution under test, pass through a suitable filter of 0.45-µm pore size, and collect the filtrate by discarding the first few milliliters. Replace with about 10 mL of *Medium*.

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

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

$A_U$ = 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)

$V$ = volume of *Medium*, 950 mL

$L$ = label claim of mesalamine (mg/Tablet)

**Tolerances:** NMT 1% of the labeled amount of mesalamine ($C_7H_7NO_3$) is dissolved.

**Buffer stage 2**

**Standard solution:** 0.025 mg/mL of USP Mesalamine RS in *Medium*. Sonicate to dissolve, if necessary.

**Sample solution:** At the specified *Times*, withdraw about 10 mL of the solution under test, pass through a suitable filter of 0.45-µm pore size, and collect the filtrate by discarding the first few milliliters. Dilute 2.0 mL of the filtrate with *Medium* to 100 mL. Replace with about 10 mL of *Medium*.

**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 ($i$):

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

$A_U$ = 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*, 50

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 (*i*) (mg/mL)

$V$ = volume of *Medium*, 960 mL

$L$ = label claim (mg/Tablet)

$V_S$ = volume of the solution under test withdrawn at each time point (*i*) during *Buffer stage 2*, 10 mL

**Tolerances:** See *Table 5*.

**Table 5**

| Time Point (*i*) | Time (h) | Amount Dissolved (%) |
|---|---|---|
| 1 | 1 | NMT 30 |
| 2 | 2 | 20–60 |
| 3 | 6 | NLT 80 |

**Test 5:** If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 5*.

**Medium**

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

**Buffer stage 1:** pH 6.4 phosphate buffer (prepare a solution of 6.8 g/L of potassium phosphate, monobasic and 0.55 g/L of sodium hydroxide in water, and adjust with either 2.5 N sodium hydroxide solution or phosphoric acid to a pH of 6.4); 950 mL, deaerated

**Buffer stage 2:** pH 7.2 phosphate buffer (after withdrawing 40 mL of solution from *Buffer stage 1* at the specified *Times*, add 50 mL of 0.4 N sodium hydroxide solution to the remaining solution, and adjust with either 4 N sodium hydroxide or phosphoric acid to a pH of 7.2); 960 mL

**Apparatus 2:** 100 rpm

**Times**

**Acid stage:** 2 h

**Buffer stage 1:** 1 h

**Buffer stage 2:** 1, 2, and 6 h

**Diluent:** pH 7.2 phosphate buffer prepared as follows. Prepare a solution of 6.8 g/L of potassium phosphate, monobasic and 1.3 g/L of sodium hydroxide in water, and adjust with either 0.4 N sodium hydroxide solution or phosphoric acid to a pH of 7.2.

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

**Acid stage**

**Standard solution:** 0.016 mg/mL of USP Mesalamine RS in *Medium, Acid stage* from *Standard stock solution*

**Sample solution:** Place 1 Tablet in each vessel containing *Medium, Acid stage*. At the specified *Time*, withdraw 10 mL of the solution under test. Pass through a suitable filter of 0.45-µm pore size and discard the first 5 mL of the filtrate. Drain the remaining *Medium, Acid stage* and retain the Tablet in the respective vessel.

**Instrumental conditions**

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

**Mode:** UV

**Analytical wavelength:** 302 nm

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

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

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

$A_U$ = 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)

$V$ = volume of *Medium*, 750 mL

$L$ = label claim (mg/Tablet)

**Tolerances:** See *Table 6*.

**Buffer stage 1**

**Standard solution:** 0.012 mg/mL of USP Mesalamine RS in *Medium, Buffer stage 1* from *Standard stock solution*

**Sample solution:** After draining the *Medium, Acid stage*, transfer *Medium, Buffer stage 1* to each dissolution vessel already containing the Tablet from the *Acid stage*. At the specified *Time*, withdraw 40 mL of the solution and proceed immediately as directed in *Buffer stage 2*. Pass through a suitable filter of 0.45-µm pore size and discard the first 5 mL of the filtrate.

**Instrumental conditions**

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

**Mode:** UV

**Analytical wavelength:** 330 nm

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

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

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

$A_U$ = 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*, 950 mL

$L$ = label claim (mg/Tablet)

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

**Tolerances:** See *Table 6*.

**Table 6**

| Level | Number Tested | Acceptance Criteria |
|---|---|---|
| $L_1$ | 6 | No individual value exceeds 1% dissolved. |
| $L_2$ | 6 | Average of the 12 units ($L_1 + L_2$) is NMT 1% dissolved, and no individual unit is >2.5% dissolved. |
| $L_3$ | 12 | Average of the 24 units ($L_1 + L_2 + L_3$) is NMT 1% dissolved, and no individual unit is >2.5% dissolved. |

**Buffer stage 2**

**Standard solution:** 0.04 mg/mL of USP Mesalamine RS in *Diluent* from *Standard stock solution*

**Sample stock solution:** Continue the test from *Buffer stage 1*. Add 50 mL of 0.4 N sodium hydroxide solution to each dissolution vessel. Adjust with either 4 N sodium hydroxide or phosphoric acid to a pH of 7.2 and start the dissolution for *Buffer stage 2*. At the specified *Times*, withdraw about 10 mL (for manual sampling) or 7 mL (for autosampler) of the solution under test and replace with 10 mL (for manual sampling) or 7 mL (for autosampler) of *Medium* for *Buffer stage 2*. Pass through a suitable filter of 0.45-µm pore size and discard the first 5 mL of the filtrate. The nominal concentration of the solution is about 1.25 mg/mL of mesalamine.

**Sample solution:** Nominally 0.0375 mg/mL of mesalamine in *Diluent* from *Sample stock solution*. Pass through a suitable filter of 0.45-µm pore size and discard the first 5 mL of the filtrate.

**Instrumental conditions**

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

**Mode:** UV

**Analytical wavelength:** 330 nm

**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*):

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

$A_U$ = 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*, 33.3

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

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

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

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

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

$V$ = volume of *Medium*, 960 mL

$L$ = label claim (mg/Tablet)

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

$Q_B$ = percentage of the labeled amount of mesalamine dissolved in *Buffer stage 1*

$V_S$ = volume of the *Sample solution* withdrawn at each time point, 10 mL (for manual sampling) or 7 mL (for autosampler)

**Tolerances:** See *Table 7*.

**Table 7**

| Time Point (*i*) | Time (h) | Amount Dissolved (%) |
|---|---|---|
| 1 | 1 | NMT 22 |
| 2 | 2 | 35–60 |
| 3 | 6 | 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*.

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

**IMPURITIES**

***Change to read:***

• **Organic Impurities**

▲**Buffer, Mobile phase, Sample stock solution,** and **Sample solution:** Prepare as directed in the *Assay*.

**Standard solution:** 0.002 mg/mL of USP Mesalamine RS in 0.01 N hydrochloric acid

**Sensitivity solution:** 0.1 µg/mL of USP Mesalamine RS in 0.01 N hydrochloric acid, prepared from *Standard solution*

**Chromatographic system**

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

**Mode:** LC

**Detector:** UV 220 nm

**Column:** 4.6-mm × 25-cm; 5-µm packing L7

**Column temperature:** 30°

**Flow rate:** 1.5 mL/min

**Injection volume:** 30 µL

**Run time:** NLT 2.8 times the retention time of mesalamine

**System suitability**

**Samples:** *Standard solution* and *Sensitivity 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 Tablets 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 0.10%

**Total degradation products:** NMT 2.0%▲ (USP 1-Dec-2024)

**ADDITIONAL REQUIREMENTS**

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

***Change to read:***

• **USP Reference Standards** ⟨11⟩

USP Mesalamine RS

▲▲ (USP 1-Dec-2024)

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| MESALAMINE DELAYED-RELEASE TABLETS | Documentary Standards Support | SM22020 Small Molecules 2 |

**Chromatographic Database Information:** Chromatographic Database

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