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Niacin Extended-Release Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click <https://www.uspnf.com/rb/niacin-ert-20200731>.

DEFINITION

Niacin Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of niacin ($C_6H_5NO_2$).

IDENTIFICATION

- **A.** 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

Diluent: Methanol and water (82:18)

Mobile phase: Methanol and water (82:18), adjusted with glacial acetic acid to a pH of 3.15 ± 0.05

Standard solution: 250 µg/mL of [USP Niacin RS](#), 50 µg/mL of [USP 6-Hydroxynicotinic Acid RS](#), and 97.8 µg/mL of pyridine in *Diluent*

Sample solution: Transfer a quantity of powder, equivalent to 50 mg of niacin from NLT 20 finely powdered Tablets, to a suitable flask, add *Diluent*, and stir for 2 h. Dilute with *Diluent* to a final concentration of 250 µg/mL of niacin.

Chromatographic system

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

Mode: LC

Detector: UV 260 nm

Column: 4.6-mm × 15-cm; 5-µm packing L8

Flow rate: 1.0 mL/min

Injection volume: 25 µL

System suitability

Sample: *Standard solution*

[NOTE—See

▲ [Table 14](#) ▲ (RB 1-Aug-2020) for relative retention times.]

Suitability requirements

Resolution: NLT 1.5 between pyridine and 6-hydroxynicotinic acid, and NLT 1.5 between 6-hydroxynicotinic acid and niacin

Relative standard deviation: NMT 3.0% for each of the peaks

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of niacin ($C_6H_5NO_2$) in the portion of Tablets taken:

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

r_U = peak area of niacin from the *Sample solution*

r_S = peak area of niacin from the *Standard solution*

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

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS**Change to read:**

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

Test 1

Medium: Water; 900 mL

Apparatus 1: 100 rpm

Times: 1, 3, 6, 9, 12, and 20 h; without *Medium* replacement. [NOTE—Withdraw the same volume at each time point.]

Solution A: Solution of sodium heptanesulfonate in acetic acid, methanol, and water (4:44:33:19), w/w¹

Mobile phase: Mixture of methanol, water, and *Solution A* (560:440:25)

Standard solution: [USP Niacin RS](#) at a known concentration in water in the range of 75–750 µg/mL

Sample solution: Filtered portion of the solution under test suitably diluted with *Medium* if necessary

Chromatographic system

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

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 15-cm; 10-µm packing L1

Flow rate: 1.0 mL/min

Injection volume: 15 µL

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*

Determine, in mg/mL, the content of niacin ($C_6H_5NO_2$) in the *Medium* at each time point:

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

r_U = peak area of niacin from the *Sample solution*

r_S = peak area of niacin from the *Standard solution*

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

D = dilution factor for the *Sample solution*

Calculate the percentage of the labeled amount of niacin ($C_6H_5NO_2$) dissolved at each time point:

At 1 h:

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

At 3 h:

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

At 6 h:

$$\text{Result}_3 = [C_3 \times (V - 2 \times V_S) + (C_1 + C_2) \times V_S] \times 100/L$$

At 9 h:

$$\text{Result}_4 = [C_4 \times (V - 3 \times V_S) + (C_1 + C_2 + C_3) \times V_S] \times 100/L$$

At 12 h:

$$\text{Result}_5 = [C_5 \times (V - 4 \times V_S) + (C_1 + C_2 + C_3 + C_4) \times V_S] \times 100/L$$

At 20 h:

$$\text{Result}_6 = [C_6 \times (V - 5 \times V_S) + (C_1 + C_2 + C_3 + C_4 + C_5) \times V_S] \times 100/L$$

C = as $C_1, C_2, \dots, C_6$, the content of niacin in the *Medium* at each time point (mg/mL)



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V = volume of *Medium*, 900 mL

V_s = volume of sample withdrawn at each time point (mL)

L = label claim (mg/Tablet)

Tolerances: The percentage of the labeled amount of niacin ($C_6H_5NO_2$) dissolved at the times specified in [Table 1](#), [Table 2](#), and [Table 3](#) conforms to [Dissolution <711>](#), [Acceptance Table 2](#).

Table 1. For Tablets Labeled to Contain 500 mg or Less/Tablet

Time (h)	Amount Dissolved (%)
1	NMT 15
3	17–32
6	33–48
9	43–63
12	52–77
20	NLT 75

Table 2. For Tablets Labeled to Contain 750 mg/Tablet

Time (h)	Amount Dissolved (%)
1	NMT 15
3	16–31
6	31–46
9	42–62
12	51–76
20	NLT 75

Table 3. For Tablets Labeled to Contain 1000 mg/Tablet

Time (h)	Amount Dissolved (%)
1	NMT 15
3	15–30
6	30–45
9	40–60
12	50–75
20	NLT 75

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; 900 mL

Buffer stage medium: 6.8 g of monobasic potassium phosphate and 0.89 g of sodium hydroxide pellets in 1000 mL of water. Adjust with diluted sodium hydroxide or phosphoric acid to a pH of 6.8; 900 mL.

Apparatus 1: 100 rpm

Times: 1, 4, 12, and 24 h: 1 and 4 h in the *Acid stage medium*; 12 and 24 h in the *Buffer stage medium*. Replace the volume withdrawn with the equal volume of medium preheated to $37 \pm 0.5^\circ$.

Procedure: After 4 h replace the *Acid stage medium* with the *Buffer stage medium*, and run the test for the times specified (additional 20 h for a total of 24 h).

[NOTE—Withdraw the same volume at each time point. Pass a portion of the solution through a suitable filter.]

Standard stock solution: 0.2 mg/mL of [USP Niacin RS](#) in water

Standard solution 1: Dilute *Standard stock solution* with *Acid stage medium* to a final concentration of 0.01 mg/mL of [USP Niacin RS](#).

Standard solution 2: Dilute *Standard stock solution* with *Buffer stage medium* to a final concentration of 0.01 mg/mL of [USP Niacin RS](#).

Sample solution

For Tablets labeled to contain 500 mg: Dilute a filtered portion of the solution under test with appropriate dissolution medium 25-fold.

For Tablets labeled to contain 750 mg: Dilute a filtered portion of the solution under test with appropriate dissolution medium 33-fold.

For Tablets labeled to contain 1000 mg: Dilute a filtered portion of the solution under test with appropriate dissolution medium 50-fold.

Instrumental conditions

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

Mode: UV

Analytical wavelength: 262 nm

Path length: 1 cm

Blank: *Acid stage medium* or *Buffer stage medium*

Analysis

Samples: *Standard solution 1* or *Standard solution 2* and *Sample solution*

Determine the concentration, in mg/mL, of niacin ($C_6H_5NO_2$) in the sample withdrawn from the vessel at each time point:

$$\text{Result} = [(A_U - A_B)/A_S] \times C_S \times D$$

A_U = absorbance of the *Sample solution*

A_B = absorbance of the *Blank*

A_S = absorbance of the *Standard solution*

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

D = dilution factor for the *Sample solution*

Calculate the percentage of the labeled amount of niacin ($C_6H_5NO_2$) dissolved at each time point:

At 1 h:

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

At 4 h:

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

At 12 h:

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

At 24 h:

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

C = as $C_1, \dots, C_4$, the content of niacin in the related dissolution medium at each time point (mg/mL)

V = volume of *Medium*, 900 mL

V_S = volume of sample withdrawn at each time point (mL)