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Buspirone Hydrochloride Tablets

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-buspirone-hcl-tabs-20210528.

DEFINITION
Buspirone Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of buspirone hydrochloride ($C_{21}H_{31}N_5O_2 \cdot HCl$).

IDENTIFICATION

- **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

  Sample: Grind 20 Tablets to a fine powder, add 50 mL of chloroform, stir for 3–5 min, and filter into a 250-mL evaporating flask. Evaporate the solution with the aid of a rotary evaporator to dryness at low heat. Use the residue.

  Acceptance criteria: Meet the requirements

- **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**

  Buffer A: 6.8 g/L of monobasic potassium phosphate and 0.93 g/L of sodium 1-hexanesulfonate monohydrate, adjusted with phosphoric acid to a pH of 3.4

  Buffer B: 3.4 g/L of monobasic potassium phosphate and 3.52 g/L of sodium 1-hexanesulfonate monohydrate, adjusted with phosphoric acid to a pH of 2.2

  Solution A: Acetonitrile and *Buffer A* (5:95)

  Solution B: Acetonitrile and *Buffer B* (75:25)

  Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	90	10
6	90	10
34	42	58
45	42	58
55	0	100
56	100	0
60	100	0
61	90	10

Diluent: *Solution A*

Impurities stock solution: 0.25 mg/mL each of USP Buspirone Related Compound A RS, USP Buspirone Related Compound G RS, USP Buspirone Related Compound K RS, USP Buspirone Related Compound L RS, and USP Buspirone Related Compound N RS in acetonitrile

System suitability solution: 1.0 mg/mL of USP Buspirone Hydrochloride RS and 0.001 mg/mL each of USP Buspirone Related Compound A RS, USP Buspirone Related Compound G RS, USP Buspirone Related Compound K RS, USP Buspirone Related Compound L RS, and USP Buspirone Related Compound N RS in *Diluent* from the *Impurities stock solution*

Standard solution: 0.1 mg/mL of USP Buspirone Hydrochloride RS in *Diluent*

Sample solution: Nominally 0.1 mg/mL of buspirone hydrochloride from NLT 20 finely powdered Tablets in *Diluent*, prepared as follows. Transfer a suitable amount of the powder to a suitable volumetric flask. Add 60% of the flask volume of *Diluent*, and sonicate for 30 min.

Allow the solution to cool to room temperature, and then dilute with *Diluent* to volume. Centrifuge the solution and filter the supernatant. Further dilute the filtrate with *Diluent* as needed.

Chromatographic system

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

Mode: LC

Detector: UV 240 nm

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

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 2.0 between the buspirone and buspirone related compound G peaks, *System suitability solution*

Tailing factor: NMT 1.5, *Standard solution*

Relative standard deviation: NMT 1.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of buspirone hydrochloride ($C_{21}H_{31}N_5O_2 \cdot HCl$) 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 Buspirone Hydrochloride RS in the *Standard solution* (mg/mL)

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

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

Change to read:

• **Dissolution ⟨711⟩**

Medium: 0.01 N hydrochloric acid; 500 mL

Apparatus 2: 50 rpm ▲with suitable sinker, if needed▲ (RB 1-Jun-2021)

Time: 30 min

Sample solution: Filter a portion of the solution under test, and dilute with *Medium* as needed.

Standard solution: USP Buspirone Hydrochloride RS in *Medium* having a concentration similar to that expected in the *Sample solution*

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum at about 235 ▲or 237▲ (RB 1-Jun-2021) nm

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of the labeled amount of buspirone hydrochloride ($C_{21}H_{31}N_5O_2 \cdot HCl$) 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 buspirone hydrochloride from the *Standard solution*

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

V = volume of *Medium*, 500 mL

L = label claim (mg/Tablet)

Tolerances: NLT 80% (Q) of the labeled amount of buspirone hydrochloride ($C_{21}H_{31}N_5O_2 \cdot HCl$) is dissolved.

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

IMPURITIES

• **Organic Impurities**

Buffer A, Buffer B, Solution A, Solution B, Mobile phase, Diluent, Impurities stock solution, and **System suitability solution:** Proceed as directed in the *Assay*.

Standard solution: 0.001 mg/mL each of USP Buspirone Hydrochloride RS, USP Buspirone Related Compound A RS, USP Buspirone Related Compound G RS, USP Buspirone Related Compound K RS, USP Buspirone Related Compound L RS, and USP Buspirone Related Compound N RS in *Diluent*

Sample solution: Nominally 1.0 mg/mL of buspirone hydrochloride from NLT 20 finely powdered Tablets in *Diluent*, prepared as follows. Transfer a suitable amount of the powder to a suitable volumetric flask. Add 60% of the flask volume of *Diluent*, and sonicate for 30 min. Allow the solution to cool to room temperature, and then dilute with *Diluent* to volume. Centrifuge the solution and filter the supernatant. Use the filtrate.

Chromatographic system

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

Mode: LC

Detector: UV 210 and 240 nm

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

Column temperature: 40°

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

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

Suitability requirements

Resolution at 240 nm: NLT 2.0 between the buspirone and buspirone related compound G peaks, *System suitability solution*

Resolution at 210 nm: NLT 4.0 between the buspirone related compound L and buspirone related compound N peaks, *System suitability solution*

Relative standard deviation: NMT 2.0% for each peak, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

For impurities detected at UV 240 nm

Calculate the percentage of buspirone related compound A in the portion of Tablets taken:

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

r_U = peak response of buspirone related compound A from the *Sample solution*

r_S = peak response of buspirone related compound A from the *Standard solution*

C_S = concentration of USP Buspirone Related Compound A RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any individual 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 individual unspecified degradation product from the *Sample solution*

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

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

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

Acceptance criteria

For impurities detected at UV 240 nm: See *Table 2*. Disregard any peak below 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Buspirone related compound A[a]	0.2	0.20
Spiroammonium salt[b,c]	0.3	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Bispyrimidinylpiperazinyl butane[c,d]	0.6	—
Bispyrimidinylpiperazinylbutyl ether[c,e]	0.7	—
Buspirone open ring[c,f]	0.8	—
Buspirone open ring dimer[c,g]	0.9	—
Buspirone	1.0	—
Buspirone related compound G[c,h]	1.05	—
Buspirone diester dimer[c,i]	1.1	—
Chlorobuspirone[c,j]	1.2	—
Buspirone open ring spirodimer[c,k]	1.5	—
Any individual unspecified degradation product	—	0.2
Total impurities	—	See *Table 3*

[a] 2-(Piperazin-1-yl)pyrimidine.

[b] 8-(Pyrimidin-2-yl)-8-aza-5-azoniaspiro[4.5]decane.

[c] Process impurity included for identification only and not included in the calculation of total degradation products.

[d] 1,4-Bis[4-(pyrimidin-2-yl)piperazin-1-yl]butane.

[e] Bis{4-[1-(pyrimidine-2-yl)piperazine-4-yl]butane-1-yl} ether.

[f] 2-{1-[2-Oxo-2-({4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl}amino)ethyl]cyclopentyl}acetic acid.

[g] 4-[4-(Pyrimidin-2-yl)piperazin-1-yl]butyl 2-{1-[2-oxo-2-({4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl}amino)ethyl]cyclopentyl}acetate.

[h] 1,4-Di(pyrimidin-2-yl)piperazine.

[i] Bis{4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl} 2,2′-(cyclopentane-1,1-diyl)diacetate.

[j] 8-{4-[4-(5-Chloropyrimidin-2-yl)piperazin-1-yl]butyl}-8-azaspiro[4.5]decane-7,9-dione.

[k] 4-(7,9-Dioxo-8-azaspiro[4.5]decan-8-yl)butyl 2-{1-[2-oxo-2-({4-[4-(pyrimidin-2-yl)piperazin-1-yl]butyl}amino)ethyl]cyclopentyl}acetate.

For impurities detected at UV 210 nm

Calculate the percentage of any individual 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 individual unspecified degradation product from the *Sample solution*

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

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

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

Acceptance criteria

For impurities detected at UV 210 nm: See *Table 3*. Disregard any peak below 0.05%.

Table 3

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Buspirone related compound K[a,b]	0.6	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Buspirone	1.0	—
Buspirone related compound L[b,c]	1.7	—
Buspirone bromobutyl analog[b,d]	1.8	—
Buspirone related compound N[b,e]	1.9	—
Any individual unspecified degradation product	—	0.2
Total impurities	—	2.0[f]

[a] 8-Azaspiro[4.5]decane-7,9-dione.

[b] Process impurity included for identification only and not included in the calculation of total degradation products.

[c] 8-(4-Chlorobutyl)-8-azaspiro[4.5]decane-7,9-dione.

[d] 8-(4-Bromobutyl)-8-azaspiro[4.5]decane-7,9-dione.

[e] 8,8'-(Butane-1,4-diyl)bis(8-azaspiro[4.5]decane-7,9-dione).

[f] Total impurities include impurities detected at UV 240 nm.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Buspirone Hydrochloride RS

USP Buspirone Related Compound A RS
2-(Piperazin-1-yl)pyrimidine.
$C_8H_{12}N_4$ 164.21

USP Buspirone Related Compound G RS
1,4-Di(pyrimidin-2-yl)piperazine.
$C_{12}H_{14}N_6$ 242.28

USP Buspirone Related Compound K RS
8-Azaspiro[4.5]decane-7,9-dione.
$C_9H_{13}NO_2$ 167.21

USP Buspirone Related Compound L RS
8-(4-Chlorobutyl)-8-azaspiro[4.5]decane-7,9-dione.
$C_{13}H_{20}ClNO_2$ 257.76

USP Buspirone Related Compound N RS
8,8'-(Butane-1,4-diyl)bis(8-azaspiro[4.5]decane-7,9-dione).
$C_{22}H_{32}N_2O_4$ 388.50

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

Topic/Question	Contact	Expert Committee
BUSPIRONE HYDROCHLORIDE TABLETS	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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