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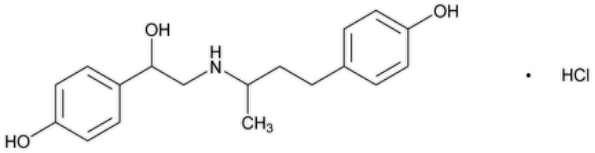
Ractopamine Hydrochloride Suspension



$C_{18}H_{23}NO_3 \cdot HCl$ 337.84

Benzenemethanol, 4-hydroxy-α-[[[3-(4-hydroxyphenyl)-1-methylpropyl]amino]methyl]-, hydrochloride;

(±)-all-*rac*-*p*-Hydroxy-α-[[[3-(*p*-hydroxyphenyl)-1-methylpropyl]amino]methyl]benzyl alcohol, hydrochloride CAS RN®: 90274-24-1; UNII: 309G9J93TP.

DEFINITION

Ractopamine Hydrochloride Suspension contains NLT 10% and NMT 20%, by weight, of ractopamine hydrochloride ($C_{18}H_{23}NO_3 \cdot HCl$) in water.

[Note—The material partially precipitates out at room temperature to form a slurry, and redissolves when heated to 50°–60°.]

IDENTIFICATION

Change to read:

• ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (CN 1-May-2020)

Sample: Dry a portion of Ractopamine Hydrochloride Suspension under vacuum for 3 h at 60°.

ASSAY

• **Procedure**

Solution A: 5.75 mg/mL solution of monobasic ammonium phosphate adjusted with 10% phosphoric acid to a pH of 4.0 ± 0.1

Solution B: 1.1 mg/mL solution of 1-heptanesulfonic acid sodium salt in *Solution A*

Mobile phase: Stabilizer-free tetrahydrofuran and *Solution B* (3:17)

Diluent: Stabilizer-free tetrahydrofuran and water (3:17). [Note—The *Standard solutions* and *System suitability solution* are stable for up to 72 h at room temperature. The *Sample solution* is stable for up to 90 h at room temperature.]

System suitability solution: 100 µg/mL of USP Ractopamine Hydrochloride RS and 10 µg/mL of USP Raspberry Alcohol RS in *Diluent*

Standard solution A: 0.08 mg/mL of USP Ractopamine Hydrochloride RS in *Diluent*

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

Standard solution C: 0.12 mg/mL of USP Ractopamine Hydrochloride RS in *Diluent*

Sample stock solution: Stir Ractopamine Hydrochloride Suspension in a 60° water bath for up to 1 h, to ensure complete dissolution. While hot, transfer 700 mg of the Ractopamine Hydrochloride Suspension dropwise to a 100-mL volumetric flask, and dilute with *Diluent* to volume.

Sample solution: Dilute a portion of the *Sample stock solution* with *Diluent* (1:10).

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

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

Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

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

Suitability requirements

Resolution: NLT 1.5 between raspberry alcohol and ractopamine, *System suitability solution*

Tailing factor: NLT 0.7 and NMT 2.0 for the ractopamine peak, *Standard solution B*

Relative standard deviation: NMT 2.0% for three replicate injections, *Standard solution B*

Analysis

Samples: *Standard solutions* and *Sample solution*

Prepare a calibration curve using the three ractopamine peak responses from *Standard solutions A, B,* and *C* and their corresponding concentrations. From the graph determine the concentration, C, in mg/mL, of ractopamine hydrochloride in the *Sample solution*.

Calculate the percentage (w/w) of $C_{18}H_{23}NO_3 \cdot HCl$ in the portion of Ractopamine Hydrochloride Suspension taken:

$$\text{Result} = (V/W) \times C_S \times D \times 100$$

V = volume of the *Sample stock solution*, 100 mL

W = weight of Ractopamine Hydrochloride Suspension taken (mg)

C_S = concentration of ractopamine hydrochloride from the *Sample solution*

D = dilution factor to prepare the *Sample solution*, 10

Acceptance criteria: 10%–20% of $C_{18}H_{23}NO_3 \cdot HCl$

IMPURITIES

Organic Impurities

- **Procedure**

Solution A: 5.75 mg/mL of monobasic ammonium phosphate in water; pH NLT 4.4

Solution B: 1.1 mg/mL of 1-heptanesulfonic acid sodium salt in *Solution A*

Solution C: Acetonitrile and *Solution B* (1:9)

Solution D: Acetonitrile and *Solution B* (17:33)

Mobile phase: See the gradient table below.

Time (min)	Solution C (%)	Solution D (%)
0	100	0
22	0	100
32	0	100
37	100	0
55	100	0

Diluent: Acetonitrile and water (1:4)

System suitability solution: 9 µg/mL each of USP Raspberry Ketone RS and USP Ractopamine Hydrochloride RS in *Diluent*

Blank: *Diluent*

Sample solution A: Stir Ractopamine Hydrochloride Suspension in a 60° water bath for up to 1 h, to ensure complete dissolution. While hot, transfer 200 mg of the Ractopamine Hydrochloride Suspension dropwise into a 50-mL volumetric flask, and dilute with *Diluent* to volume.

Sample solution B: Dilute a portion of *Sample solution A* with *Diluent* (1:100). [Note—The *Sample solutions* are stable for up to 48 h if stored at 5°.]

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

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

Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NLT 2.0 between raspberry ketone and ractopamine

Analysis

Samples: *Blank*, *Sample solution A*, and *Sample solution B*

[NOTE—Disregard any peaks that correspond to those in the *Blank*. Correct the response of the ractopamine peak in *Sample solution B* by subtracting the peak response at the retention time of ractopamine in the *Blank*.]

Calculate the percentage of each individual impurity in the portion of Ractopamine Hydrochloride Suspension taken:

$$\text{Result} = (r_A/r_B) \times 100/D$$

r_A = peak response of each individual impurity from *Sample solution A*

r_B = corrected peak response for ractopamine from *Sample solution B*

D = dilution factor to prepare *Sample solution B,* 100

Acceptance criteria

Individual impurities: See *Impurity Table 1.*

Total impurities: NMT 3.5%

Impurity Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Octopamine[a]	0.37	0.5
Tyramine[b]	0.55	0.5
N-Isopropyloctopamine[c]	0.63	0.5
Piperazinediphenol[d]	0.74	0.5
Aminobutylphenol[e]	0.76	0.5
Raspberry alcohol[f]	0.85	0.5
Raspberry ketone[g]	0.96	1.0
Ractopamine	1.0	—
Deoxyractopamine[h]	1.1	0.5
Ractopamine *O*-methyl[i]	1.2	1.0
Ractopamine *N*-hydroxy benzyl[j]	1.26	1.0
Ractopamine cyclohexyl analog[k]	1.29	0.5
Ractopamine dimer[l]	1.4	1.0
Any individual unspecified impurity	—	0.2

[a] 4-(2-Amino-1-hydroxyethyl)phenol.

[b] 4-(2-Aminoethyl)phenol.

[c] 4-[1-Hydroxy-2-(isopropylamino)ethyl]phenol.

[d] 4,4'-(Piperazine-2, 5-diyl)diphenol.

[e] 4-(3-Aminobutyl)phenol.

[f] 4-(3-Hydroxybutyl)phenol.

[g] 4-(4-Hydroxyphenyl)butan-2-one.

[h] 4-[3-(4-Hydroxyphenethylamino)butyl]phenol.

[i] 4-{3-[2-(4-Hydroxyphenyl)-2-methoxyethylamino]butyl}phenol.

[j] 4-(1-Hydroxy-2-{(4-hydroxybenzyl)[4-(4-hydroxyphenyl)butan-2-yl]amino}ethyl)phenol.

[k] 4-{1-Hydroxy-2-[3-(4-hydoxyphenyl)-5-methylcyclo hexylamino]ethyl}phenol).

[l] 4,4'-(1,1'-Oxybis{2-[4-(4-hydroxyphenyl)butan-2-ylamino]ethane-1,1-diyl})diphenol.

SPECIFIC TESTS

• **Diastereomer Ratio**

Solution A: 5.75 mg/mL of monobasic ammonium phosphate in water

Solution B: Add 10 mL of triethylamine to 950 mL of *Solution A*, dilute with *Solution A* to 1000 mL, and adjust with phosphoric acid to a pH of 4.5.

Mobile phase: Acetonitrile and *Solution B* (3:22)

Diluent: Acetonitrile and *Solution A* (1:4)

System suitability solution: 0.4 mg/mL of USP Ractopamine Hydrochloride RS in *Diluent*

Sample solution: Stir Ractopamine Hydrochloride Suspension in a 60° water bath for up to 1 h to ensure complete dissolution. While hot, transfer 275 mg of it dropwise into a 100-mL volumetric flask, and dilute with *Diluent* to volume.

[Note—The *Sample solution* is stable for up to 36 h when stored at ambient conditions.]

Chromatographic system

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

Mode: LC

Detector: UV 226 nm

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

Flow rate: 1 mL/min

Injection size: 20 µL

System suitability

Sample: *System suitability solution*

[Note—The elution order is *RS,SR* diastereoisomer followed by *RR,SS* diastereoisomer.]

Suitability requirements

Resolution: NLT 1.25 between the diastereomers

Analysis

Sample: *Sample solution*

Calculate the *RS,SR* diastereomer content, in percentage:

$$\text{Result} = r_A/(r_A + r_B) \times 100$$

r_A = peak response of the *RS,SR* diastereoisomer from the *Sample solution*

r_B = peak response of the *RR,SS* diastereoisomer from the *Sample solution*

Acceptance criteria: 45%–49%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Store at a temperature not exceeding 70°.

• **Labeling:** Label it to indicate that it is for veterinary use only.

• **USP Reference Standards ⟨11⟩**

USP Ractopamine Hydrochloride RS

USP Raspberry Alcohol RS

4-(3-Hydroxybutyl)phenol.

$C_{10}H_{14}O_2$ 166.22

USP Raspberry Ketone RS

4-(4-Hydroxyphenyl)butan-2-one.

$C_{10}H_{12}O_2$ 164.20

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

Topic/Question	Contact	Expert Committee
RACTOPAMINE HYDROCHLORIDE SUSPENSION	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
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