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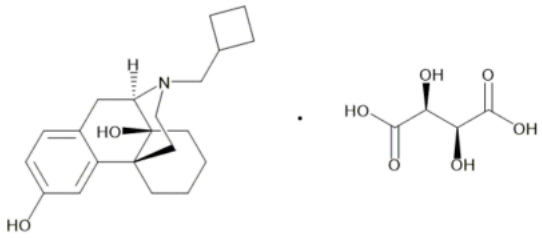
Butorphanol Tartrate



$C_{21}H_{29}NO_2 \cdot C_4H_6O_6$ 477.55

Morphinan-3,14-diol, 17-(cyclobutylmethyl)-, (−)-, [*S*-(*R**,*R**)]-2,3-dihydroxybutanedioate (1:1) (salt);

(−)-17-(Cyclobutylmethyl)morphinan-3,14-diol D-(−)-tartrate (1:1) (salt) CAS RN®: 58786-99-5; UNII: 2L7I72RUHN.

DEFINITION

Butorphanol Tartrate contains NLT 98.0% and NMT 102.0% of butorphanol tartrate ($C_{21}H_{29}NO_2 \cdot C_4H_6O_6$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** ▲197A or▲ (USP 1-May-2022) 197K

Change to read:

• **B.** ▲The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.▲ (USP 1-May-2022)

ASSAY

Change to read:

• **Procedure**

▲**Buffer:** 0.025 M of monobasic potassium phosphate in water

Mobile phase: Acetonitrile, triethylamine, and *Buffer* (15: 5.1: 85). Adjust with phosphoric acid to a pH of 3.0.

Standard solution: 0.1 mg/mL of USP Butorphanol Tartrate RS in water

Sample solution: 0.1 mg/mL of Butorphanol Tartrate in water

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 4.6-mm × 25-cm; 5-µm packing L11

Column temperature: 40°

Flow rate: 2.0 mL/min

Injection volume: 60 µL

Run time: NLT 1.4 times the retention time of butorphanol

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 0.73%

Tailing factor: NMT 2.0

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of butorphanol tartrate ($C_{21}H_{29}NO_2 \cdot C_4H_6O_6$) in the portion of Butorphanol Tartrate taken:

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

r_U = peak response of butorphanol from the *Sample solution*

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

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

C_U = concentration of Butorphanol Tartrate in the *Sample solution* (mg/mL)

▲ (USP 1-May-2022)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Delete the following:

▲• **Organic Impurities, Procedure 1**

Standard solution: 1 mg/mL of USP Butorphanol Tartrate RS in methanol

Sample solution: 10 mg/mL of Butorphanol Tartrate in methanol

Chromatographic system

(See *Chromatography ⟨621⟩, General Procedures, Thin-Layer Chromatography*.)

Mode: TLC

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 50 µL of *Sample solution*, 5 µL and 10 µL of *Standard solution*

Developing solvent system: Chloroform, methanol, benzene, and ammonium hydroxide (85:25:20:5)

Iodoplatinate spray reagent: Prepare a 1-in-10 solution of chloroplatinic acid in water. To 0.5 mL of this solution, add 33 mL of water and 1 g of potassium iodide. Prepare fresh daily.

Analysis

Samples: *Standard solution* and *Sample solution*

Apply 50 µL of the Sample solution, containing 500 µg of butorphanol tartrate, and 5 µL and 10 µL of the Standard solution, containing 5 µg and 10 µg of USP Butorphanol Tartrate RS, respectively, about 2 cm apart to a line parallel to and about 2 cm from the bottom of the thin-layer chromatographic plate. Develop the chromatogram until the solvent front has moved about 10 cm above the line of application. Remove the plate, mark the solvent front, and allow the solvent to evaporate. Spray the plate with *Iodoplatinate spray reagent*. Estimate the percentage of the impurities present in the Sample solution by comparing the intensities of secondary spots, if present, with the intensities of the principal spots obtained from the chromatograms of the Standard solution.

Acceptance criteria

Total impurities: NMT 2.0%▲ (USP 1-May-2022)

Delete the following:

▲• **Organic Impurities, Procedure 2**

Sample solution: 10 mg/mL of Butorphanol Tartrate in methanol

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 1.8-m × 4-mm; glass column containing 3% liquid phase G3 on support S1AB

Temperatures

Injector: 280°

Column: 250°

Detector: 290°

Carrier gas: Nitrogen

Injection volume: 1 µL

System suitability

Sample: *Sample solution*

Suitability requirements

Relative retention time for the alpha isomer of butorphanol tartrate: 1.2, relative to butorphanol tartrate

Retention time of butorphanol tartrate: NLT 15 min

Analysis

Sample: *Sample solution*

Record a 30-min chromatogram. Preferably using an electronic integrator, determine the areas of all peaks in the chromatogram excluding the area of the solvent.

Calculate the percentage of synthesis precursors in the portion of Butorphanol Tartrate taken:

$$\text{Result} = (r_V/r_S) \times 100$$

r_V = sum of the peak responses of all minor peaks

r_S = sum of the peak responses of the major and minor peaks

Acceptance criteria: NMT 2.0%▲ (USP 1-May-2022)

Add the following:

▲• **Organic Impurities**

Buffer and **Mobile phase:** Prepare as directed in the *Assay*.

Sensitivity solution: 0.5 µg/mL of USP Butorphanol Tartrate RS in water

Standard solution: 1.0 µg/mL of USP Butorphanol Tartrate RS in water

Sample solution: 1.0 mg/mL of Butorphanol Tartrate in water

Chromatographic system: Proceed as directed in the *Assay*, except for the *Run time*.

Run time: NLT 4 times the retention time of butorphanol

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 individual impurity in the portion of Butorphanol Tartrate taken:

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

r_U = peak response of any individual impurity from the *Sample solution*

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

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

C_U = concentration of Butorphanol Tartrate in the *Sample solution* (mg/mL)

Acceptance criteria: The reporting threshold is 0.05%.

Any unspecified impurity: NMT 0.10%

Total impurities: NMT 0.5%▲ (USP 1-May-2022)

SPECIFIC TESTS

• **Optical Rotation** ⟨781S⟩, *Procedures, Specific Rotation*

Sample solution: 4 mg/mL of Butorphanol Tartrate in methanol

Acceptance criteria: −60° to −66°

• **Water Determination** ⟨921⟩, *Method I*: NMT 2.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers. Store at 25°, excursions permitted between 15° and 30°.

• **USP Reference Standards** ⟨11⟩

USP Butorphanol Tartrate RS

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

Topic/Question	Contact	Expert Committee
BUTORPHANOL TARTRATE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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