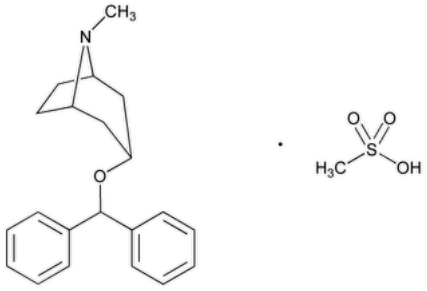
Status: Currently Official on 13-Feb-2025
Official Date: Official as of 01-Jul-2021
Document Type: USP Monographs
DocId: GUID-8C510CB0-E6DB-454D-AE5D-404B7998C381_5_en-US
DOI: https://doi.org/10.31003/USPNF_M8500_05_01
DOI Ref: jh3i1

Benztropine Mesylate

To view the Notice from the Expert Committee that posted in conjunction with this accelerated revision, please click https://www.uspnf.com/rb-benztropine-mesylate-20210625.



$C_{21}H_{25}NO \cdot CH_4O_3S$ 403.54

8-Azabicyclo[3.2.1]octane, 3-(diphenylmethoxy)-*N*-methyl-, *endo*-, methanesulfonate;

3α-(Diphenylmethoxy)-1α*H*,5α*H*-tropane methanesulfonate;

(1*R*,3*r*,5*S*)-3-(Benzhydryloxy)-8-methyl-8-azabicyclo[3.2.1]octane methanesulfonate CAS RN®: 132-17-2.

DEFINITION

Benztropine Mesylate contains NLT 98.0% and NMT 102.0% of benztropine mesylate ($C_{21}H_{25}NO \cdot CH_4O_3S$), calculated on the dried basis.

IDENTIFICATION

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

Solution A: 2.7 g/L of monobasic potassium phosphate in water. Adjust with phosphoric acid to a pH of 3.2.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	75	25
6	75	25
10	30	70
10.1	75	25
17	75	25

Diluent: Acetonitrile and water (30:70)

System suitability solution: 500 µg/mL of USP Benztropine Mesylate RS and 5 µg/mL of USP Benztropine Related Compound A RS in *Diluent*

Standard solution: 500 µg/mL of USP Benztropine Mesylate RS in *Diluent*

Sample solution: 500 µg/mL of Benztropine Mesylate in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 2.1-mm × 15-cm; 1.7-µm packing L43. [NOTE—A guard column with similar packing may be used.]

Flow rate: 0.3 mL/min

Injection volume: 2 µL

System suitability

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

[NOTE—The relative retention times for benztropine related compound A and benztropine are 0.9 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.3 between benztropine related compound A and benztropine, *System suitability solution*

Tailing factor: NMT 3.0, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of benztropine mesylate ($C_{21}H_{25}NO \cdot CH_4O_3S$) in the portion of Benztropine Mesylate 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 Benztropine Mesylate RS in the *Standard solution* (µg/mL)

C_U = concentration of Benztropine Mesylate in the *Sample solution* (µg/mL)

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

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%

Change to read:

• **ORGANIC IMPURITIES**

Solution A, Solution B, Diluent, System suitability solution, Sample solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	75	25
6	75	25
25	45	55
26	30	70
27	30	70
27.1	75	25
36	75	25

Sensitivity solution: 0.25 µg/mL of USP Benztropine Mesylate RS in *Diluent*

Standard solution: 0.5 µg/mL of USP Benztropine Mesylate RS and 1 µg/mL each of USP Benztropine Related Compound A RS, USP Benzhydrol RS, and USP Benzophenone RS in *Diluent*

System suitability

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

[NOTE—See *Table 3* for the relative retention times.]

Suitability requirements

Resolution: NLT 1.3 between benztropine related compound A and benztropine, *System suitability solution*

Relative standard deviation: NMT 5.0% for benztropine, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Sample solution* and *Standard solution*

Calculate the percentage of benztropine related compound A, benzhydrol, or benzophenone in the portion of Benztropine Mesylate taken:

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

r_U = peak response of benztropine related compound A, benzhydrol, or benzophenone from the *Sample solution*

r_S = peak response of the corresponding Reference Standard from the *Standard solution*

C_S = concentration of the corresponding Reference Standard in the *Standard solution* (µg/mL)

C_U = concentration of Benztropine Mesylate in the *Sample solution* (µg/mL)

Calculate the percentage of diphenylmethane or any individual unspecified impurity in the portion of Benztropine Mesylate taken:

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

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

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

C_S = concentration of USP Benztropine Mesylate RS in the *Standard solution* (µg/mL)

C_U = concentration of Benztropine Mesylate in the *Sample solution* (µg/mL)

F = relative response factor (see *Table 3*)

Acceptance criteria: See *Table 3*. The reporting threshold is 0.05%.

Table 3

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Benztropine related compound A	0.9	—	▲0.3▲ (RB 1-Jul-2021)
Benztropine	1.0	—	—
Benzhydrol	1.6	—	0.10
Benzophenone	2.4	—	0.10
Diphenylmethane	3.2	2.2	0.10
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	0.50

SPECIFIC TESTS

- **Loss on Drying** ⟨731⟩

Analysis: Dry at 105° for 2 h.

Acceptance criteria: NMT 5.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.
- **USP Reference Standards** ⟨11⟩

USP Benzhydrol RS

Diphenylmethanol.

$C_{13}H_{12}O$ 184.24

USP Benzophenone RS

Benzophenone; also known as Diphenylmethanone.

$C_{13}H_{10}O$ 182.22

USP Benztropine Mesylate RS

USP Benztropine Related Compound A RS

(1*R*,3*r*,5*S*)-3-(Benzhydryloxy)-8-azabicyclo[3.2.1]octane hydrochloride.

$C_{20}H_{23}NO \cdot HCl$ 329.87

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

Topic/Question	Contact	Expert Committee
BENZTROPINE MESYLATE	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 44(3)

Current DocID: GUID-8C510CB0-E6DB-454D-AE5D-404B7998C381_5_en-US

DOI: https://doi.org/10.31003/USPNF_M8500_05_01

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