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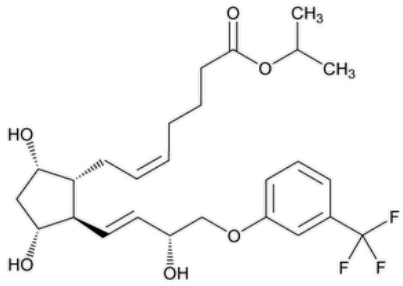
Travoprost



$C_{26}H_{35}F_3O_6$ 500.55

[1*R*-[1α(*Z*),2β(1*E*,3*R**),3α,5α]]-7-[3,5-Dihydroxy-2-[3-hydroxy-4-[3-(trifluoromethyl)phenoxy]-1-butenyl] cyclopentyl]-5-heptenoic acid, 1-methylethyl ester;

Isopropyl (*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(1*E*,3*R*)-3-hydroxy-4-[(α,α,α-trifluoro-*m*-tolyl)oxy]-1-butenyl] cyclopentyl]-5-heptenoate CAS RN®: 157283-68-6; UNII: WJ68R08KX9.

DEFINITION

Travoprost contains NLT 96.0% and NMT 102.0% of travoprost ($C_{26}H_{35}F_3O_6$), calculated on the anhydrous and solvent-free basis.

[**Caution—**Great care should be taken to avoid contact with the body.]

IDENTIFICATION

• **A. Thin-Layer Chromatographic Identification Test ⟨201⟩**

Standard solution: Use USP Travoprost RS.

Sample solution: Prepare as directed in the *Assay*.

Chromatographic system

Adsorbent: Chromatographic plate coated with silica gel that contains 20% silver nitrate

Application volume: 5 µL. [Note—To keep the spot size small, it is usually necessary to apply approximately 1–2 µL at a time, allowing the spot to dry between each application.]

Developing solvent system: Ethyl acetate and ethanol (4:1)

Spray reagent: 20% phosphomolybdic acid in ethanol

Analysis

Samples: *Standard solution* and *Sample solution*

Proceed as directed in the chapter. Spray the plate with *Spray reagent*, and heat it in an oven at 80°–100°. The travoprost will appear as black spots.

Acceptance criteria: Meets 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: Add 2.0 mL of phosphoric acid to 1 L of water. Adjust with sodium hydroxide to a pH of 3.0.

Mobile phase: Acetonitrile and *Buffer* (3:7)

Standard solution: Use USP Travoprost RS without dilution (0.5 mg/mL).

Sample solution: Transfer 25 mg of Travoprost to a 50-mL volumetric flask, and dissolve in 15 mL of acetonitrile. Add 25 mL of water, mix, and wait until the solution reaches room temperature. Dilute with water to volume, and mix.

Chromatographic system

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

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 5-cm; packing L1

Flow rate: 3.0 mL/min

Injection volume: 100 µL

System suitability

Sample: *Standard solution*

[NOTE—USP Travoprost RS contains a small percentage of the 5,6-*trans* isomer. The relative retention times for travoprost and the 5,6-*trans* isomer are about 1.0 and 1.1, respectively.]

Suitability requirements

Resolution: NLT 1.5 between travoprost and the 5,6-*trans* isomer

Column efficiency: NLT 1500 theoretical plates

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of travoprost ($C_{26}H_{35}F_3O_6$) in the portion of Travoprost taken:

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

r_U = peak area from the *Sample solution*

r_S = peak area from the *Standard solution*

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

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

Acceptance criteria: 96.0%–102.0% on the anhydrous and solvent-free basis

IMPURITIES

• **ORGANIC IMPURITIES**

Buffer, Mobile phase, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Travoprost taken:

$$\text{Result} = (r_U/r_T) \times (1/F) \times 100$$

r_U = peak response for each individual impurity

r_T = sum of the responses of all the peaks

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Travoprost related compound A	0.11	1.0	0.2
Epoxide derivative[a]	0.55	1.0	0.4
15-*epi* Diastereomer[b]	0.90	1.1	0.1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
5,6-*trans* Isomer[c]	1.16	1.0	3.5
15-Keto derivative[d]	1.45	1.6	0.3
Any other individual impurity	—	—	0.1
Total impurities	—	—	4.0

[a] (5*Z*)-(9*S*,11*R*,15*S*)-9,11,15-Trihydroxy-13,14-epoxy-16-(*m*-trifluoro methylphenoxy)-17,18,19,20-tetranor-5-prostadienoic acid, isopropyl ester.

[b] (5*Z*,13*E*)-(9*S*,11*R*,15*S*)-9,11,15-Trihydroxy-16-(*m*-trifluoromethyl phenoxy)-17,18,19,20-tetranor-5,13-prostadienoic acid, isopropyl ester.

[c] (5*E*,13*E*)-(9*S*,11*R*,15*R*)-9,11,15-Trihydroxy-16-(*m*-trifluoromethyl phenoxy)-17,18,19,20-tetranor-5,13-prostadienoic acid, isopropyl ester.

[d] (5*Z*,13*E*)-(9*S*,11*R*)-9,11-Dihydroxy-15-oxo-16-(*m*-trifluoromethyl phenoxy)-17,18,19,20-tetranor-5,13-prostadienoic acid, isopropyl ester.

- **Limit of Ethyl Acetate**

Standard solution: 50 µg/mL of ethyl acetate in *N,N*-dimethylacetamide

Sample solution: 0.02 g/mL of Travoprost in *N,N*-dimethylacetamide

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 30-m; 1-µm coating G16

Carrier gas: Helium

Temperatures

Injector port: 140°

Detector: 240°

Column: See *Table 2*.

Table 2

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
55	0	55	6
55	25	240	20

Flow rate: 4 mL/min

Injection volume: 1 µL

System suitability

Sample: *Standard solution*

[Note—The retention time for ethyl acetate is about 2–5 min.]

Suitability requirements

Resolution: NLT 1.5 between ethyl acetate and any adjacent peak

Relative standard deviation: NMT 15.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the concentration, in ppm, of ethyl acetate in the portion of Travoprost taken:

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

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of ethyl acetate in the *Standard solution* (µg/mL)

C_U = concentration of Travoprost in the *Sample solution* (g/mL)

Acceptance criteria: NMT 5000 ppm

SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation*⟨781S⟩

  Sample solution: 20 mg/mL in dehydrated alcohol

  Acceptance criteria: +52.0° to +58.0° at 365 nm

- **Water Determination,** *Method Ia*⟨921⟩

  Sample: 0.2 g

  Solvent: Acetonitrile and methanol (1:1)

  Titrant: Use a titrant for which 1 mL is equivalent to 2 mg of water.

  Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve at −25° to −15° in tight, light-resistant containers under a nitrogen atmosphere.
- **USP Reference Standards** ⟨11⟩

  USP Travoprost RS

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

Topic/Question	Contact	Expert Committee
TRAVOPROST	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

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