• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Sotalol Hydrochloride RS

Sotalol Hydrochloride Tablets

» Sotalol Hydrochloride Tablets contain not less than 95.0 percent and not more than 105.0 percent of the labeled amount of sotalol hydrochloride ($C_{12}H_{20}N_2O_3S \cdot HCl$).

Packaging and storage—Preserve in well-closed containers, and store at controlled room temperature.

USP Reference standards ⟨11⟩**—**
USP Sotalol Hydrochloride RS

Identification—Weigh and powder a quantity of the Tablets, equivalent to about 250 mg of sotalol hydrochloride, and transfer to a 50-mL volumetric flask. Add 25 mL of methanol, and shake for 10 minutes. Dilute with methanol to volume, mix, and filter: the filtrate so obtained meets the requirements for *Identification* test *B* under *Sotalol Hydrochloride.*

Dissolution ⟨711⟩**—**

Medium: water; 900 mL.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Procedure—Determine the amount of $C_{12}H_{20}N_2O_3S \cdot HCl$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 230 nm on filtered portions of the solution under test, in comparison with a Standard solution having a known concentration of USP Sotalol Hydrochloride RS in the same *Medium.*

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{12}H_{20}N_2O_3S \cdot HCl$ is dissolved in 30 minutes.

Uniformity of dosage units ⟨905⟩**:** meet the requirements.

Assay—

Phosphate buffer—Dissolve 6.8 g of monobasic potassium phosphate in about 800 mL of water. Dilute with water to 1000 mL, and mix.

Mobile phase—Prepare a filtered and degassed mixture of *Phosphate buffer* and acetonitrile (9:1).

Internal standard solution—Transfer about 1.8 g of caffeine, accurately weighed, to a 1000-mL volumetric flask. Dissolve in and dilute with water to volume, and mix.

Standard preparation—Transfer about 80 mg of USP Sotalol Hydrochloride RS, accurately weighed, to a 25-mL volumetric flask. Add 2.5 mL of 1 N hydrochloric acid, dissolve in and dilute with water to volume, mix, and filter. Transfer 10.0 mL of the filtrate and 25.0 mL of the *Internal standard solution* to a 200-mL volumetric flask. Dilute with water to volume, and mix.

Assay preparation—Transfer an appropriate number of Tablets, equivalent to about 800 mg of sotalol hydrochloride, to a 250-mL volumetric flask. Add 25 mL of 1 N hydrochloric acid, and swirl. Dilute with water to about three-fourths of the volume of the flask, and shake for 15 minutes. Dilute with water to volume, mix, and filter. Transfer 10.0 mL of this solution and 25.0 mL of the *Internal standard solution* to a 200-mL volumetric flask. Dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 238-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation,* and record the peak areas as directed for *Procedure:* the relative retention times for sotalol and caffeine are about 1.0 and 2.0, respectively; the resolution, *R,* between caffeine and sotalol is not less than 6.0; and the relative standard deviation for replicate injections, determined from peak area ratios, is not more than 2.0%.

Procedure—Separately inject equal volumes (about 25 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in mg, of sotalol hydrochloride ($C_{12}H_{20}N_2O_3S \cdot HCl$) in the portion of Tablets taken by the formula:

$$5000C(R_U / R_S)$$

in which *C* is the concentration, in mg per mL, of USP Sotalol Hydrochloride RS in the *Standard preparation;* and R_U and R_S are the peak area ratios of sotalol to caffeine obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Soybean Oil

[8001-22-7].

DEFINITION

Soybean Oil is the refined fixed oil obtained from the seeds of the soya plant *Glycine max* Merr. (Fam. Fabaceae). It may contain suitable antioxidants.

IDENTIFICATION

• **A. IDENTITY BY FATTY ACID COMPOSITION**
Analysis: Proceed as directed in the test for *Fats and Fixed Oils, Fatty Acid Composition.*
Acceptance criteria: Meets the composition profile of fatty acids in *Table 1*

• **B. IDENTITY BY TRIGLYCERIDE PROFILE**
Analysis: Proceed as directed in *Identification of Fixed Oils by Thin-Layer Chromatography* ⟨202⟩.
Acceptance criteria: Meets the requirements in the chapter

IMPURITIES

Delete the following:

•• **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 10 µg/g •• (Official 1-Jan-2018)

• **ALKALINE IMPURITIES**
Sample: 10 mL
Analysis: Mix 10 mL of acetone and 0.3 mL of water, and add 0.05 mL of bromophenol blue TS. If necessary, neutralize the solution to a green color with 0.01 N hydrochloric acid or 0.01 N sodium hydroxide. Add the *Sample*, shake, and allow to stand. Titrate with 0.01 N hydrochloric acid VS to change the color of the upper layer to yellow.
Acceptance criteria: NMT 0.1 mL of 0.01 N hydrochloric acid is required.

SPECIFIC TESTS

• **FATS AND FIXED OILS,** *Acid Value* ⟨**401**⟩**:** NMT 0.3

• **FATS AND FIXED OILS,** *Peroxide Value* ⟨**401**⟩
Solution A: Glacial acetic acid and chloroform (60:40)
Solution B: Prepare a saturated solution of potassium iodide in freshly boiled and cooled water, and store it protected from light. Discard it if it gives a color on addition of *Solution A* and starch TS.

Sample: 10 g
Titrimetric system
(See *Titrimetry* ⟨541⟩.)
Mode: Direct titration
Titrant: 0.01 N sodium thiosulfate VS
Endpoint detection: Visual
Analysis: Transfer the *Sample* to a conical flask. Add 30 mL of *Solution A*, and swirl to dissolve. Add 0.5 mL of *Solution B*, swirl the flask for 1 min, accurately timed, and add 30 mL of water. Titrate with *Titrant*, with vigorous agitation, to a light yellow color. Add 0.5 mL of starch TS, and continue the titration until the blue color has disappeared. Perform a blank test, and make any necessary correction.
Calculate the peroxide value:

$$\text{Result} = [(V \times N)/W] \times F$$

V = volume of sodium thiosulfate (mL)
N = normality of the sodium thiosulfate solution (mEq/mL)
W = weight of Soybean Oil taken (g)
F = conversion factor, 1000 g/kg
Acceptance criteria: NMT 10.0

- **FATS AND FIXED OILS,** *Fatty Acid Composition* ⟨**401**⟩**:** Soybean Oil exhibits the composition profile of fatty acids shown in *Table 1*, as determined in the chapter.

Table 1

Carbon-Chain Length	Number of Double Bonds	Percentage (%)
<14	0	≤0.1
14	0	≤0.2
16	0	9.0–13.0
16	1	≤0.3
18	0	2.5–5.0
18	1	17.0–30.0
18	2	48.0–58.0
18	3	5.0–11.0
20	0	≤1.0
20	1	≤1.0
22	0	≤1.0
22	1	≤0.3
24	0	≤0.5

- **FATS AND FIXED OILS,** *Unsaponifiable Matter* ⟨**401**⟩**:** NMT 1.5%
- **STEROL COMPOSITION**
Sample A: Transfer 5 g of Soybean Oil to a 250-mL conical flask, add 50 mL of an alcoholic potassium hydroxide solution prepared by dissolving 12 g of potassium hydroxide in 10 mL of water and diluting with alcohol to 100 mL, and heat the flask on a steam bath under a suitable condenser to maintain reflux for 1 h, swirling frequently. Cool to a temperature below 25°, and transfer the contents of the flask to a separator with a polytetrafluoroethylene stopcock, rinsing the flask with two 50-mL portions of water that are added to the separator (do not use grease on the stopcock). Extract with three 100-mL portions of ether, combining the ether extracts in another separator containing 40 mL of water. Gently rotate or shake the separator for a few minutes. [NOTE—Violent agitation may result in the formation of a difficult-to-separate emulsion.] Allow the mixture to separate, and discard the lower aqueous phase. Wash the ether extract with two additional 40-mL portions of water, and discard the lower aqueous phase. Wash the ether extract successively with a 40-mL portion of potassium hydroxide solution (3 in 100) and a 40-mL portion of water. Repeat this potassium hydroxide solution–water wash sequence three times. Wash the ether extract with 40-mL portions of water until the last washing is not reddened by the addition of 2 drops of phenolphthalein TS. Transfer the ether extract to a tared flask, and rinse the separator with 10 mL of ether, adding the rinsings to the flask. Evaporate the ether on a steam bath, and add 6 mL of acetone to the residue. Remove the acetone in a current of air, and dry the residue at 105°.
Reference A: Transfer 5 g of sunflower oil to a 250-mL conical flask, and proceed as directed in *Sample A*, beginning with "add 50 mL of an alcoholic potassium hydroxide solution prepared by dissolving 12 g of potassium hydroxide in 10 mL of water and diluting with alcohol to 100 mL".
Separation of the sterol fraction by LC
Mobile phase: Isopropyl alcohol and *n*-hexane (1:99)
Sample solution A: Transfer *Sample A* with three 4-mL quantities of ether to a 15-mL test tube. Evaporate to dryness under a stream of nitrogen. Dissolve *Sample A* in *Mobile phase* to obtain a solution with an approximate concentration of 40 mg/mL. Add a few drops of isopropyl alcohol to improve the solubility. [NOTE—3 drops are normally sufficient to ensure complete solubilization.] Pass through a membrane filter (nominal 0.45-µm pore size).
Reference solution A: Prepare as directed for *Sample solution A* except use *Reference A* instead of *Sample A*.
Chromatographic system
(See *Chromatography* ⟨621⟩.)
Mode: LC
Detector: UV 210 nm
Columns
Guard: 4.6-mm × 0.5-cm (or 4.6-mm × 1.0-cm); 5-µm packing L3 with a 6-nm pore size
Analytical: 4.6-mm × 25-cm; 5-µm packing L3 with a 6-nm pore size
Flow rate: 1.0 mL/min
Injection volume: 50 µL
Identification of peaks due to sterols
Samples: *Sample solution A* and *Reference solution A*
Sterol identification: The sterol fraction elutes at the end of the chromatogram. Locate the fraction to be collected by using the chromatogram from *Reference solution A*. The chromatogram from *Reference solution A* shows two or three principal peaks, which elute at approximately 21–35 min depending on the column used.
Sterol collection: Collect the fraction at the detector outlet in a 15-mL tube with a screw cap. Evaporate the solvent under a stream of nitrogen. [NOTE—If necessary, to increase the sample amount for later analysis, make the second injection of 50 µL on the HPLC column and collect the fraction at the detector outlet in the same 15-mL test tube with a screw cap. Evaporate the solvent under a stream of nitrogen.]
Determination of sterols by GC
Sample solution B: Dissolve the residue of the sterol fraction obtained from *Sample solution A* in the previous LC step in 0.2 mL of anhydrous pyridine and 0.2 mL of a mixture of 1 volume of chlorotrimethylsilane and 99 volumes of bis(trimethylsilyl)trifluoroacetamide. Insert the stopper into the test tube tightly and heat at 80° for 20 min. Allow to cool and use the liquid phase.
Reference solution B: Dissolve 9 parts of the residue of the sterol fraction obtained from *Reference solution A* in the previous LC step, 1 part of cholesterol in 0.2 mL of anhydrous pyridine, and 0.2 mL of a mixture of 1 volume of chlorotrimethylsilane and 99 volumes of bis(trimethylsilyl)trifluoroacetamide. Insert the stopper into the test tube tightly, and heat at 80° for 20 min. Allow to cool and use the liquid phase.

Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: GC
Detector: Flame ionization
Column: 0.25-mm × 30-m fused-silica capillary; 0.25-µm layer of phase G27
Temperatures
Injection port: 290°
Detector: 290°
Column: See *Table 2*.

Table 2

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
260	—	260	38
260	5	290	5

Carrier gas: Helium
Flow rate: 2.6 mL/min
Injection volume: 1–3 µL (depending on the expected amount of sterols in the test sample).
Injection type: Split injection; split ratio is 25:1
System suitability
Sample: *Reference solution B*
The chromatogram from *Reference solution B* shows five principal peaks corresponding to cholesterol, campesterol, stigmasterol, β-sitosterol, and Δ7-stigmastenol.
[NOTE—The retention times of the sterols with reference to β-sitosterol are given in *Table 3*.]

Table 3

Identification	Relative Retention Time
Cholesterol	0.65
Brassicasterol	0.71
24-Methylene-cholesterol	0.81
Campesterol	0.82
Campestanol	0.84
Stigmasterol	0.88
Δ7-Campesterol	0.93
Δ5,23-Stigmastadienol	0.95
Clerosterol	0.96
β-Sitosterol	1.00
Sitostanol	1.02
Δ5-Avenasterol	1.03
Δ5,24-Stigmastadienol	1.09
Δ7-Stigmastenol	1.13
Δ7-Avenasterol	1.17

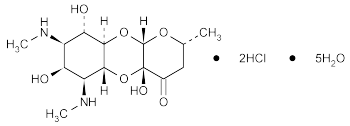
Suitability requirements
Resolution: NLT 3.0 between the campesterol and stigmasterol peaks
Analysis
Samples: *Sample solution B* and *Reference solution B*
Use the chromatogram from *Reference solution B* to identify the peaks due to cholesterol, campesterol, stigmasterol, β-sitosterol and Δ7-stigmastenol. Identify the peaks due to the sterols in the chromatogram from *Sample solution B* using the chromatograms from *Reference solution B* and the relative retention times with reference to β-sitosterol (main peak) given in *Table 3*.
Calculate the percentage of the content of each sterol in the sterol fraction of Soybean Oil taken:

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

r_U = area of the peak due to the sterol component to be determined
r_T = sum of the areas of the peaks due to the components indicated in *Table 3*
Acceptance criteria: NMT 0.3% of brassicasterol
- **WATER DETERMINATION,** *Method Ic* ⟨**921**⟩**:** NMT 0.1%

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers, and avoid exposure to excessive heat.
- **LABELING:** Label it to indicate the name and quantity of any added antioxidant. Where Soybean Oil is intended for use in the manufacture of injectable dosage forms, it is so labeled.
- **OTHER REQUIREMENTS:** For Soybean Oil intended for use in injectable dosage forms, which is specified in the labeling, the requirements for *Unsaponifiable Matter*, *Acid Value*, *Peroxide Value*, and *Water, Method Ic* in *Injections and Implanted Drug Products* ⟨1⟩*, Specific Tests, Vehicles and added substances, Nonaqueous vehicles* must be met.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Soybean Oil RS

Spectinomycin Hydrochloride



$C_{14}H_{24}N_2O_7 \cdot 2HCl \cdot 5H_2O$ 495.35
4*H*-Pyrano[2,3-*b*][1,4]benzodioxin-4-one, decahydro-4a,7,9-trihydroxy-2-methyl-6,8-bis(methylamino)-, dihydrochloride, pentahydrate, [2*R*-(2α,4a*β*,5a*β*,6*β*,7*β*,8*β*,9α,9aα,10a*β*)]-.
(2*R*,4a*R*,5a*R*,6*S*,7*S*,8*R*,9*S*,9a*R*,10a*S*)-Decahydro-4a,7,9-trihydroxy-2-methyl-6,8-bis(methylamino)-4*H*-pyrano[2,3-*b*]1,4]benzodioxin-4-one dihydrochloride pentahydrate [22189-32-8].
Anhydrous 405.28 [21736-83-4].

» Spectinomycin Hydrochloride has a potency equivalent to not less than 603 µg of spectinomycin ($C_{14}H_{24}N_2O_7$) per mg.

Packaging and storage—Preserve in tight containers.
Labeling—Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.
USP Reference standards ⟨11⟩**—**
USP Spectinomycin Hydrochloride RS
USP Endotoxin RS
Identification, *Infrared Absorption* ⟨197M⟩**—**Do not dry specimen.
Crystallinity ⟨695⟩: meets the requirements.
Bacterial Endotoxins Test ⟨85⟩**—**Where the label states that Spectinomycin Hydrochloride is sterile or that it must be subjected to further processing during the preparation of injectable dosage forms, it contains not more than 0.09 USP Endotoxin Unit per mg of spectinomycin.
Sterility Tests ⟨71⟩**—**Where the label states that Spectinomycin Hydrochloride is sterile, it meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined*.
pH ⟨791⟩: between 3.8 and 5.6, in a solution containing 10 mg per mL.
Water Determination, *Method I* ⟨921⟩: between 16.0% and 20.0%.