sum of all peak areas in the *Sample solution*, except for the major peak, is not greater than twice the major peak area of the *Standard solution* (1.0%).

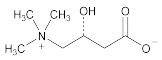
SPECIFIC TESTS

- **OPTICAL ROTATION,** *Specific Rotation* ⟨**781S**⟩**:** –102° to –106° at 20°
  Sample solution: 10 mg/mL in methanol
- **LOSS ON DRYING** ⟨**731**⟩**:** Dry about 1.000 g of the sample at 105° to constant weight: it loses NMT 0.5% of its weight.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Protect from light.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Levocabastine Hydrochloride RS
  USP Levocabastine Related Compound A RS

Levocarnitine



$C_7H_{15}NO_3$ 161.20

(*R*)-3-Carboxy-2-hydroxy-*N*,*N*,*N*-trimethyl-1-propanaminium, inner salt;
(*R*)-(3-Carboxy-2-hydroxypropyl)trimethylammonium, inner salt [541-15-1].

DEFINITION

Levocarnitine contains NLT 97.0% and NMT 103.0% of levocarnitine ($C_7H_{15}NO_3$), calculated on the anhydrous basis.

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨**197K**⟩
  Analysis: Dry the sample and the USP Levocarnitine RS under vacuum at 50° for 5 h.
  Acceptance criteria: Meets the requirements

ASSAY

- **PROCEDURE**
  Sample: 100 mg of Levocarnitine
  Blank: A mixture of 3 mL of formic acid and 50 mL of glacial acetic acid
  Titrimetric system
  (See *Titrimetry* ⟨541⟩.)
  Mode: Direct titration
  Titrant: 0.1 N perchloric acid VS
  Endpoint detection: Visual
  Analysis: Dissolve the *Sample* in a mixture of 3 mL of formic acid and 50 mL of glacial acetic acid. Add 2 drops of crystal violet TS, and titrate with the *Titrant* to an emerald green endpoint. Perform the *Blank* determination.
  Calculate the percentage of levocarnitine ($C_7H_{15}NO_3$) in the portion of Levocarnitine taken:

$$\text{Result} = \{[(V_S - V_B) \times N \times F]/W\} \times 100$$

V_S = *Titrant* volume consumed by the *Sample* (mL)
V_B = *Titrant* volume consumed by the *Blank* (mL)
N = actual normalilty of the *Titrant* (mEq/mL)
F = equivalency factor, 161.2 mg/mEq
W = *Sample* weight (mg)

Acceptance criteria: 97.0%–103.0% on the anhydrous basis

IMPURITIES

- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.5%
- **CHLORIDE AND SULFATE,** *Chloride* ⟨**221**⟩
  Standard: 0.50 mL of 0.020 N hydrochloric acid
  Sample: 0.090 g of Levocarnitine
  Acceptance criteria: NMT 0.4%
- **HEAVY METALS** ⟨**231**⟩**:** NMT 20 ppm
- **LIMIT OF POTASSIUM**
  [NOTE—The *Standard solution* and the *Sample solutions* may be modified, if necessary, to obtain solutions of suitable concentrations adaptable to the linear or working range of the instrument.]
  Standard solution: 31.25 µg/mL of potassium in water, prepared from potassium chloride, previously dried at 105° for 2 h
  Sample stock solution: 0.625 mg/mL of Levocarnitine in water
  Sample solution A: Transfer 20.0 mL of the *Sample stock solution* to a 25-mL volumetric flask, and dilute with water to volume. This solution contains 500 µg/mL of Levocarnitine and 0 µg/mL of added potassium from the *Standard solution*.
  Sample solution B: Transfer 20.0 mL of the *Sample stock solution* to a 25-mL volumetric flask, add 2.0 mL of the *Standard solution*, and dilute with water to volume. This solution contains 500 µg/mL of Levocarnitine and 2.5 µg/mL of added potassium from the *Standard solution*.
  Sample solution C: Transfer 20.0 mL of the *Sample stock solution* to a 25-mL volumetric flask, add 4.0 mL of the *Standard solution*, and dilute with water to volume. This solution contains 500 µg/mL of Levocarnitine and 5.0 µg/mL of added potassium from the *Standard solution*.
  Blank: Water
  Instrumental conditions
  (See *Spectrophotometry and Light-Scattering* ⟨851⟩.)
  Mode: Atomic absorption spectrophotometry
  Analytical wavelength: 766.7 nm
  Lamp: Potassium hollow-cathode
  Flame: Air–acetylene
  Analysis
  Samples: *Sample solution A*, *Sample solution B*, *Sample solution C*, and *Blank*
  Determine the absorbances of the solutions against the *Blank*. Plot the absorbances of the three *Sample solutions* versus their added potassium concentrations, in µg/mL. Draw the straight line best fitting the three points, and extrapolate the line until it intercepts the concentration axis. From the intercept determine the concentration, in µg/mL, of potassium in *Sample solution A*.
  Calculate the percentage of potassium in the portion of Levocarnitine taken:

$$\text{Result} = (C_K/C_U) \times 100$$

C_K = concentration of potassium in *Sample solution A* (µg/mL), determined from the intercept of the linear regression line
C_U = concentration of Levocarnitine in *Sample solution A* (µg/mL)

  Acceptance criteria: NMT 0.2%
- **LIMIT OF SODIUM**
  [NOTE—The *Standard solution* and the *Sample solutions* may be modified, if necessary, to obtain solutions of suitable concentrations adaptable to the linear or working range of the instrument.]
  Standard solution: 250 µg/mL of sodium in water, prepared from sodium chloride, previously dried at 105° for 2 h
  Sample stock solution: 40.0 mg/mL of Levocarnitine in water
  Sample solution A: Transfer 20.0 mL of the *Sample stock solution* to a 25-mL volumetric flask, and dilute with water

to volume. This solution contains 32 mg/mL of Levocarnitine and 0 µg/mL of added sodium from the *Standard solution*.
Sample solution B: Transfer 20.0 mL of the *Sample stock solution* to a 25-mL volumetric flask, add 2.0 mL of the *Standard solution*, and dilute with water to volume. This solution contains 32 mg/mL of Levocarnitine and 20 µg/mL of added sodium from the *Standard solution*.
Sample solution C: Transfer 20.0 mL of the *Sample stock solution* to a 25-mL volumetric flask, add 4.0 mL of the *Standard solution*, and dilute with water to volume. This solution contains 32 mg/mL of Levocarnitine and 40 µg/mL of added sodium from the *Standard solution*.
Blank: Water
Instrumental conditions
(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)
Mode: Atomic absorption spectrophotometry
Analytical wavelength: 589.0 nm
Lamp: Sodium hollow-cathode
Flame: Air–acetylene
Analysis
Samples: *Sample solution A*, *Sample solution B*, *Sample solution C*, and *Blank*
Determine the absorbances of the solutions against the *Blank*. Plot the absorbances of the three *Sample solutions* versus their added sodium concentrations, in µg/mL. Draw the straight line best fitting the three points, and extrapolate the line until it intercepts the concentration axis. From the intercept determine the concentration, in µg /mL, of sodium in *Sample solution A*.
Calculate the percentage of sodium in the portion of Levocarnitine taken:

$$\text{Result} = (C_{Na}/C_U) \times 100$$

C_{Na} = concentration of sodium in *Sample solution A* (µg/mL), determined from the intercept of the linear regression line
C_U = concentration of Levocarnitine in *Sample solution A* (µg/mL)
Acceptance criteria: NMT 0.1%

SPECIFIC TESTS
- **Optical Rotation,** *Specific Rotation* ⟨**781S**⟩
Sample solution: 100 mg/mL in water
Acceptance criteria: −29° to −32°
- **pH** ⟨**791**⟩
Sample solution: 50 mg/mL solution
Acceptance criteria: 5.5–9.5
- **Water Determination** ⟨**921**⟩**:** NMT 4.0%

ADDITIONAL REQUIREMENTS
- **Packaging and Storage:** Preserve in tight containers.
- **USP Reference Standards** ⟨**11**⟩
USP Levocarnitine RS
USP Levocarnitine Related Compound A RS
2-Propen-1-aminium, 3-carboxy-*N*,*N*,*N*-trimethyl-, chloride.
$C_7H_{14}ClNO_2$ 179.65

Levocarnitine Injection

» Levocarnitine Injection is a sterile solution of Levocarnitine in Water for Injection. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_7H_{15}NO_3$.

Packaging and storage—Preserve in single-dose containers, preferably of Type I glass. Store below 25°. Do not freeze.

USP Reference standards ⟨11⟩**—**
USP Endotoxin RS
USP Levocarnitine RS
USP Levocarnitine Related Compound A RS
2-Propen-1-aminium, 3-carboxy-*N*,*N*,*N*-trimethyl-, chloride.
$C_7H_{14}ClNO_2$ 179.65

Identification—

A: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

B: Transfer 2 mL of Injection to a test tube, add 5 mL of 1 N hydrochloric acid and a few drops of ammonium reineckate TS: a red-violet precipitate is produced.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 0.1 USP Endotoxin Unit per mg of levocarnitine.

pH ⟨791⟩: between 6.0 and 6.5.

Particulate matter ⟨788⟩: meets the requirements for small-volume injections.

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—

0.05 M Phosphate buffer—Dissolve 6.805 g of monobasic potassium phosphate in 1000 mL of water.

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile and *0.05 M Phosphate buffer* (65:35). Adjust with phosphoric acid to a pH of 4.7, and mix. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Levocarnitine RS in water to obtain a solution having a known concentration of about 10 mg per mL.

System suitability solution—Dissolve accurately weighed quantities of USP Levocarnitine RS and USP Levocarnitine Related Compound A RS in water to obtain a solution having concentrations of about 5.0 mg per mL and 0.024 mg per mL, respectively.

Assay preparation—Pool the contents of ten containers, and dilute an accurately measured volume of Injection quantitatively with water to obtain a solution having a concentration of about 10 mg of levocarnitine per mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 205-nm detector and a 3.9-mm × 30-cm column that contains packing L8. The flow rate is maintained at about 1 mL per minute. The system is programmed to provide variable mixtures of acetonitrile, *Mobile phase*, and water. Initially elute 50 mL of acetonitrile, then change the composition linearly over the next 20 minutes to a mixture of 65% acetonitrile and 35% water. Elute 100 mL of this mixture, then change the composition linearly over the following 20 minutes to 100% *Mobile phase*, and allow the chromatograph to proceed for about 3 hours. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure:* the resolution, *R,* between levocarnitine related compound A and levocarnitine is not less than 1.0; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 5 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of levocarnitine ($C_7H_{15}NO_3$) in the portion of Injection taken by the formula:

$$(CL / D)(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Levocarnitine RS in the *Standard preparation; L* is the labeled quantity, in mg, of levocarnitine in each container; D is the concentration, in mg per mL, of levocarnitine in the *Assay preparation*, based on the labeled quantity per container and the extent of dilution; and r_U and r_S are the levocarnitine peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.