Status: Currently Official on 17-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-EC7209AA-4E3A-4D93-8305-6C1E6490A184_3_en-US
DOI: https://doi.org/10.31003/USPNF_M13610_03_01
DOI Ref: i7buz

Carprofen Tablets

» Carprofen Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of carprofen ($C_{15}H_{12}ClNO_2$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—

USP Carprofen RS

Identification—

Change to read:

A: ▲*Spectroscopic Identification Tests ⟨197⟩, Infrared Spectroscopy: 197K*▲ (CN 1-May-2020) —

Reference specimen—Mix about 2 mg of USP Carprofen RS with 200 mg of potassium bromide, and grind thoroughly for 10 to 15 minutes. Compress the mixture into a clear pellet. Record the IR spectrum of the pellet immediately after preparation.

Test specimen—Grind into powder not fewer than 4 Tablets. Transfer the powder, equivalent to about 100 mg of carprofen, to a 125-mL separatory funnel. Add 30 mL of water and 3 drops of hydrochloric acid, and shake for about 5 minutes. Add about 30 mL of methylene chloride, and shake for another 5 minutes. Allow the phases to separate. Carefully drain and collect the lower methylene chloride layer through anhydrous sodium sulfate that is placed on a cotton pledget into a suitable container. Evaporate the methylene chloride on a steam bath with the aid of a stream of nitrogen to dryness. Dry the residue in vacuum at 60° for about 30 minutes. Mix about 2 mg of the dried residue with 200 mg of potassium bromide, and grind thoroughly for 10 to 15 minutes. Compress the mixture into a clear pellet. Record the IR spectrum of the carprofen sample pellet immediately after preparation.

B: 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*.

Dissolution ⟨711⟩—

[Note—Use low-actinic volumetric flasks, dissolution vessels, and evaporation covers.]

Medium: 0.05 M phosphate buffer, pH 7.5 (prepared by dissolving 6.8 g of monobasic potassium phosphate in 600 mL of water, mixing, adding 18 mL of 2 N sodium hydroxide, mixing, diluting with water to 1000 mL, and adjusting with 0.2 N sodium hydroxide or 0.2 N hydrochloric acid to a pH of 7.50 ± 0.05); 900 mL, degassed.

Apparatus 2: 50 rpm.

Time: 30 minutes.

Determine the amount of $C_{15}H_{12}ClNO_2$ dissolved by employing the following method.

Standard solution—

FOR TABLETS LABELED TO CONTAIN 25 MG—Transfer about 25 mg of USP Carprofen RS, accurately weighed, to a 900-mL volumetric flask. Slowly add 10 mL of methanol. Dilute with *Medium* to volume, and mix.

FOR TABLETS LABELED TO CONTAIN 75 MG—Transfer about 75 mg of USP Carprofen RS, accurately weighed, to a 900-mL volumetric flask. Slowly add 30 mL of methanol. Dilute with *Medium* to volume, and mix.

FOR TABLETS LABELED TO CONTAIN 100 MG—Transfer about 100 mg of USP Carprofen RS, accurately weighed, to a 900-mL volumetric flask. Slowly add 40 mL of methanol. Dilute with *Medium* to volume, and mix.

Test solution—Pass a portion of the solution under test through a suitable 0.45-µm filter.

System suitability solution—Determine the absorbance of the *Standard solution,* as directed for *Procedure,* five times: the relative standard deviation is not more than 2.0%.

Procedure—Determine the amount of $C_{15}H_{12}ClNO_2$ dissolved by measuring the absorbance of the *Test solution* in comparison with the appropriate *Standard solution* at the wavelength of maximum absorbance at about 300 nm, using a 0.5-cm cell for Tablets labeled to contain 25 mg, a 0.2-cm cell for Tablets labeled to contain 75 mg, and a 0.1-cm cell for Tablets labeled to contain 100 mg. Use *Medium* as the blank. Calculate the percentage of $C_{15}H_{12}ClNO_2$ dissolved by the formula:

$$\frac{A_U \times W_S \times 100}{A_S \times LC}$$

in which A_U and A_S are the absorbances obtained from the *Test solution* and the *Standard solution,* respectively; W_S is the weight, in mg, of USP Carprofen RS used to prepare the *Standard solution;* 100 is the conversion factor to percentage; and *LC* is the Tablet label claim, in mg.

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{15}H_{12}ClNO_2$ is dissolved in 30 minutes.

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

PROCEDURE FOR CONTENT UNIFORMITY—[Note—Use low-actinic glassware.]

Mobile phase and *Chromatographic system*—Prepare as directed in the *Assay.*

Standard solution—Prepare as directed for the *Standard preparation* in the *Assay.*

Test solution—Transfer 10 Tablets individually to 10 separate volumetric flasks of a suitable calibrated volume such that an interim concentration of 0.5 mg per mL of *Mobile phase* can be prepared. To each flask, add *Mobile phase* to 80% of the calibrated volume, sonicate for 10 minutes, then stir for 10 minutes. Sonicate again for 10 minutes, and stir for another 10 minutes or until the Tablets are completely disintegrated. Cool to room temperature, dilute with *Mobile phase* to volume to obtain an interim concentration of 0.5 mg of carprofen per mL, and mix. Quantitatively transfer 5.0 mL of the individual solutions to 10 separate 50.0-mL volumetric flasks, dilute with *Mobile phase* to volume, and mix. Pass the solution through a polyvinylidenefluoride (PVDF) filter having a 0.45-µm or finer porosity, discarding the first 5 mL of the filtrate. The final concentration is about 0.05 mg of carprofen per mL.

Procedure—Proceed as directed for *Procedure* in the *Assay.* Calculate the percentage of the labeled content of $C_{15}H_{12}ClNO_2$ in the portion of Tablets taken by the formula:

$$100(C_S/C_U)(r_U/r_S)$$

in which the terms are as defined therein.

Chromatographic purity—

Mobile phase—Proceed as directed in the *Assay.*

Standard solution—[Note—Use low-actinic glassware.] Dissolve an accurately weighed quantity of USP Carprofen RS in *Mobile phase* to obtain a solution having a known concentration of 0.05 µg of carprofen per mL.

Sensitivity solution—[Note—Use low-actinic glassware.] Quantitatively dilute the *Standard solution* with *Mobile phase* to obtain a solution containing about 0.005 µg of carprofen per mL.

Test solution—Use the *Assay preparation.*

Blank solution—Transfer an accurately weighed portion of the Tablet base, equivalent to the weight of 1 Tablet, to a volumetric flask of the same calibrated volume as that used to prepare the *Test solution*. To each flask add *Mobile phase* to 80% of the calibrated volume. Sonicate for 10 minutes, then stir for 10 minutes. Sonicate again for 10 minutes, and stir for another 10 minutes. Cool to room temperature, dilute with *Mobile phase* to volume, and mix. Quantitatively transfer 5.0 mL of the solution to a 50.0-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Pass the solution through a PVDF filter having a 0.45-µm or finer porosity, discarding the first 5 mL of the filtrate.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 240-nm detector and a 4.6-mm × 15-cm column that contains 5-µm packing L7. The flow rate is about 1.0 mL per minute. Wash the column after each series of analyses with a mixture of acetonitrile and water (20:80) for 30 minutes; gradually change the composition of acetonitrile and water to 80:20 over 10 minutes; continue to wash at 80:20 for 30 minutes; gradually change the composition to 50:50 over 10 minutes; and continue to wash at 50:50 for another 30 minutes. Chromatograph the *Standard solution,* the *Sensitivity solution,* and the *Test solution,* and record the peak responses as directed for *Procedure:* for the *Standard solution,* the column efficiency is not less than 4000 theoretical plates, the tailing factor is not more than 2.0, and the relative standard deviation for replicate injections is not more than 2.0%; for the *Sensitivity solution,* the carprofen peak should be defined and integratable; for the *Test solution,* the resolution, *R,* between carprofen and the nearest impurity peak is not less than 2.0. After every six injections of any solution, inject a *Standard solution* in duplicate. The ratio of the average response of the duplicate injections to that obtained from the initial five replicate injections is 0.95 to 1.05.

Procedure—Inject a volume (about 50 µL) of the *Standard solution,* the *Test solution,* and the *Blank solution* into the chromatograph, record the chromatograms, and measure all the peak areas. Calculate the percentage of carprofen-related compounds in the portion of Tablets taken by the formula:

$$0.1(C_S/C_U)(r_i/r_S)$$

in which C_S is the concentration, in µg per mL, of carprofen in the *Standard solution;* C_U is the concentration, in mg per mL, of carprofen in the *Test solution;* r_i is the peak area of any peak other than carprofen obtained from the *Test solution;* and r_S is the peak area of carprofen obtained from the *Standard solution:* not more than 0.5% of any single impurity is found; and the sum of all impurities is not more than 2.0%. Disregard any peak also observed in the *Blank solution.*

Assay—

Mobile phase—Mix 500 mL of acetonitrile, 500 mL of water, and 1 mL of phosphoric acid. Degas before using. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—[Note—Use low-actinic glassware.] Dissolve an accurately weighed quantity of USP Carprofen RS in *Mobile phase* to obtain a solution having a known concentration of about 0.05 mg per mL.

Assay preparation—[Note—Use low-actinic glassware.] Accurately weigh 20 Tablets, and calculate the average Tablet weight. Grind the Tablets into uniform powder. Transfer three accurately weighed portions of the powder, each equivalent to the weight of one Tablet, into three volumetric flasks of a suitable calibrated volume such that an interim concentration of 0.5 mg per mL of *Mobile phase* can be prepared. To each flask add *Mobile phase* to 80% of the calibrated volume, sonicate for 10 minutes, then stir for 10 minutes. Sonicate again for 10 minutes, and stir for another 10 minutes. Cool to room temperature, dilute with *Mobile phase* to volume to obtain an interim concentration of 0.5 mg of carprofen per mL, and mix. Quantitatively transfer 5.0 mL of the solution to a 50.0-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Pass the solution through a PVDF filter having a 0.45-µm or finer porosity, discarding the first 5 mL of the filtrate. The final concentration is about 0.05 mg of carprofen per mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 240-nm detector and a 4.6-mm × 15-cm column that contains packing L7. The flow rate is about 1.0 mL per minute. Wash the column after each series of analyses with a mixture of acetonitrile and water (20:80) for 30 minutes; gradually change the composition of acetonitrile and water to 80:20 over 10 minutes; continue to wash at 80:20 for 30 minutes; gradually change the composition to 50:50 over 10 minutes; and continue to wash at 50:50 for another 30 minutes. Chromatograph the *Standard preparation,* and record the peak areas as directed for *Procedure:* the column efficiency for carprofen is not less than 4000 theoretical plates; the tailing factor is not more than 2.0; and the relative standard deviation for five replicate injections is not more than 2.0%. Inject the *Standard preparation* in duplicate after every 12 injections or fewer of any other solution. The ratio of the average area of the duplicate injections to that obtained from the initial five replicate injections is 0.95 to 1.05.

Procedure—Separately inject equal volumes (about 20 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 percentage of the labeled content of carprofen ($C_{15}H_{12}ClNO_2$) in the portion of Tablets taken by the formula:

$$100(C_S/C_U)(r_U/r_S)$$

in which C_S and C_U are the concentrations, in mg per mL, of USP Carprofen RS in the *Standard preparation* and carprofen in the *Assay preparation,* respectively; and r_U and r_S are the peak areas obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

Topic/Question	Contact	Expert Committee
CARPROFEN TABLETS	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 32(6)

Current DocID: GUID-EC7209AA-4E3A-4D93-8305-6C1E6490A184_3_en-US
Previous DocID: GUID-EC7209AA-4E3A-4D93-8305-6C1E6490A184_2_en-US
DOI: https://doi.org/10.31003/USPNF_M13610_03_01
DOI ref: i7buz