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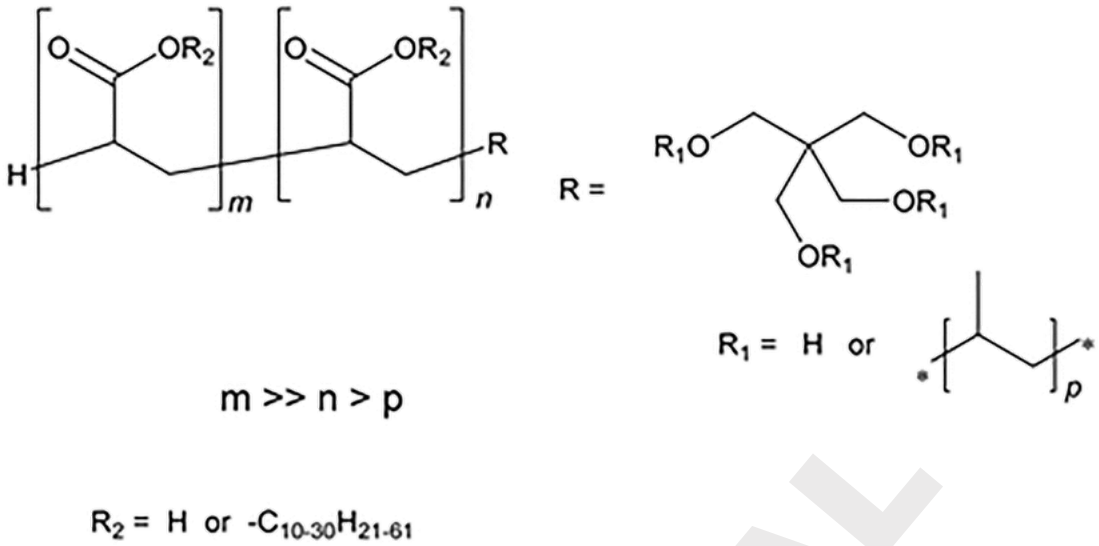
Carbomer Copolymer



DEFINITION

Carbomer Copolymer is a high molecular weight copolymer of acrylic acid and a long-chain alkyl methacrylate cross-linked with allyl ethers of pentaerythritol. Carbomer Copolymer contains NLT 52.0% and NMT 62.0% of carboxylic acid (–COOH) groups, calculated on the dried basis. [Note—The heading of this monograph does not constitute the official title for a Carbomer Copolymer manufactured with the use of benzene. When benzene is used in the manufacturing process, the name will be Carbomer 1342, provided it complies with the existing requirements in the Carbomer 1342 monograph.]

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K or 197A. The IR absorption spectrum exhibits maxima only at the same wavelengths as those of a similar preparation of USP Carbomer Copolymer RS, treated in the same manner. [Note—If peak shifting occurs during testing using the method found in 197A causing the test to fail, follow the method found in 197K.]

• **B.**

Sample: 5 g

Analysis: Add the *Sample* to 500 mL of water, and stir.

Acceptance criteria: A dispersion is formed, with a foam layer that persists after the dispersion is allowed to stand at room temperature for 1 h.

ASSAY

• **Carboxylic Acid Content**

Sample: 400 mg, previously dried under vacuum at 80° for 1 h

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Direct titration

Electrode: Calomel–glass or silver/silver chloride

Titrant: 0.25 N sodium hydroxide VS

Endpoint detection: Potentiometric

Analysis: Slowly add the *Sample* to 400 mL of water in an 800–1000-mL beaker, while stirring continually at 1000 rpm. The stirrer shaft is set at an angle of about 60° and to one side of the beaker, and the propeller is positioned near the bottom of the beaker. Continue stirring for 15 min. Allow the polymer dispersion to stand for 30 min. Transfer the beaker to a magnetic stirring device. Place an approximately 7.62-cm stirring bar into the solution, and adjust the mixer speed to obtain moderate mixing. Add 1 g of potassium chloride, and titrate with *Titrant*. After each addition of *Titrant*, allow 1 min for mixing before recording the pH.

Calculate the carboxylic acid content as a percentage of carboxylic acid groups in the portion of Carbomer Copolymer taken:

$$\text{Result} = [(V \times N_A/W) \times F] \times 100$$

V = *Titrant* volume consumed (mL)

N_A = actual normality of the *Titrant* (mEq/mL)

W = *Sample* weight (mg)

F = equivalency factor for the carboxylic acid (–COOH) group, 45.02 mg/mEq

Acceptance criteria: 52.0%–62.0%

IMPURITIES

Change to read:

• Limit of Ethyl Acetate and Cyclohexane

[Note—This test is required only for those Carbomer Copolymers where the labeling indicates that ethyl acetate or a mixture of ethyl acetate and cyclohexane was used in the polymerization process.]

Diluent: 166 mL/L of dimethyl sulfoxide in water

Standard stock solution: 7 mg/g of cyclohexane and ethyl acetate in dimethyl sulfoxide

Standard solution A: Transfer 50 ± 1 mg of Carbomer Copolymer to a 20-mL headspace vial, and add 6 mL of *Diluent* to the vial. Weigh the vial. Using a syringe, add 10 µL of the *Standard stock solution* to the vial. Weigh the vial. Calculate the weight of the added *Standard stock solution*. Seal the vial with a Teflon-lined butyl rubber septum and aluminum crimp cap. Shake the vial for 1 h.

Standard solution B: Transfer 50 ± 1 mg of Carbomer Copolymer to a 20-mL headspace vial, and add 6 mL of *Diluent* to the vial. Weigh the vial. Using a syringe, add 20 µL of the *Standard stock solution* to the vial. Weigh the vial. Calculate the weight of the added *Standard stock solution*. Seal the vial with a Teflon-lined butyl rubber septum and aluminum crimp cap. Shake the vial for 1 h.

Standard solution C: Transfer 50 ± 1 mg of Carbomer Copolymer to a 20-mL headspace vial, and add 6 mL of *Diluent* to the vial. Weigh the vial. Using a syringe, add 50 µL of the *Standard stock solution* to the vial. Weigh the vial. Calculate the weight of the added *Standard stock solution*. Seal the vial with a Teflon-lined butyl rubber septum and aluminum crimp cap. Shake the vial for 1 h.

Sample solution: Transfer 50 ± 1 mg of Carbomer Copolymer to a 20-mL headspace vial, and add 6 mL of *Diluent* to the vial. Seal the vial with a Teflon-lined septum and aluminum crimp cap. Shake for 1 h.

Chromatographic system

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

Mode: GC, equipped with a headspace injector

Detector: Flame ionization

Column: 0.53-mm × 30-m fused silica; coated with 3.0-µm stationary phase G43

Temperatures

Injection port: 140°

Detector: 250°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	—	40	10
40	30	240	5

Carrier gas: Helium

Flow rate: 5 mL/min (at a linear velocity of 35 cm/s programmed in constant pressure mode)

Injection volume: 1 mL (gaseous phase)

Injection type: Split, split ratio, 5:1

[Note—The following headspace conditions may be used: a vial pressure of 10 psi, a loop fill pressure (if equipped) of 7 psi, and a transfer line temperature of 105°.]

Vial temperature: The vials are maintained at a temperature of 80° for 45 min before headspace injection.

System suitability

Sample: *Standard solution B*

Suitability requirements

Relative standard deviation: NMT 15% from 3 injections

Analysis

Samples: ▲▲ (ERR 1-Jun-2021) *Standard solution A*, *Standard solution B*, *Standard solution C*, and *Sample solution*

The detector response factor (*RF*) of each *Standard solution* is determined by:

$$RF = (W_{SS} \times C_{SS})/(r_S - r_U)$$

W_{SS} = weight of the *Standard stock solution* added into each *Standard solution* (g)

C_{SS} = concentration of ethyl acetate or cyclohexane in *Standard stock solution* (mg/g)

r_S = peak area of ethyl acetate or cyclohexane in each *Standard solution*

r_U = peak area of ethyl acetate or cyclohexane in the *Sample solution*

Average three *RF* to obtain RF_{avg}. Calculate the percentage of ethyl acetate or cyclohexane in the portion of Carbomer Copolymer taken:

$$\text{Result} = [(RF_{avg} \times r_U)/W_U] \times 100$$

RF_{avg} = average of three *RF*

r_U = peak area of ethyl acetate or cyclohexane in the *Sample solution*

W_U = weight of Carbomer Copolymer added into the *Sample solution* (mg)

Acceptance criteria

Ethyl acetate: NMT 0.5%

Cyclohexane: NMT 0.3%

Change to read:

• **Limit of Benzene**

Diluent: 166 mL/L of dimethyl sulfoxide in water

Standard stock solution: 1.2 µg/g of benzene in dimethyl sulfoxide

Standard solution A: Transfer 50 ± 1 mg of Carbomer Copolymer to a 20-mL headspace vial, and add 6 mL of *Diluent* to the vial. Weigh the vial. Using a syringe, add 10 µL of the *Standard stock solution* to the vial. Weigh the vial. Calculate the weight of the added *Standard stock solution*. Seal the vial with a Teflon-lined butyl rubber septum and aluminum crimp cap. Shake the vial for 1 h.

Standard solution B: Transfer 50 ± 1 mg of Carbomer Copolymer to a 20-mL headspace vial, and add 6 mL of *Diluent* to the vial. Weigh the vial. Using a syringe, add 50 µL of the *Standard stock solution* to the vial. Weigh the vial. Calculate the weight of the added *Standard stock solution*. Seal the vial with a Teflon-lined butyl rubber septum and aluminum crimp cap. Shake the vial for 1 h.

Standard solution C: Transfer 50 ± 1 mg of Carbomer Copolymer to a 20-mL headspace vial, and add 6 mL of *Diluent* to the vial. Weigh the vial. Using a syringe, add 100 µL of the *Standard stock solution* to the vial. Weigh the vial. Calculate the weight of the added *Standard stock solution*. Seal the vial with a Teflon-lined butyl rubber septum and aluminum crimp cap. Shake the vial for 1 h.

Sample solution: Transfer 50 ± 1 mg of Carbomer Copolymer to a 20-mL headspace vial, and add 6 mL of *Diluent* to the vial. Seal the vial with a Teflon-lined septum and aluminum crimp cap. Shake for 1 h.

Chromatographic system

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

Mode: GC, equipped with a headspace injector

Detector: Flame ionization

Column: 0.53-mm × 30-m fused silica; coated with 3.0-µm stationary phase G46

Temperatures

Injection port: 140°

Detector: 250°

Column: See *Table 2*.

Table 2

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	—	40	10
40	30	240	5

Carrier gas: Helium

Flow rate: 5 mL/min (at a linear velocity of 35 cm/s programmed in constant pressure mode)

Injection volume: 1 mL (gaseous phase)

Injection type: Split, split ratio, 0.5: 1

[Note—The following headspace conditions may be used: a vial pressure of 10 psi, a loop fill pressure (if equipped) of 7 psi, and a transfer line temperature of 105°.]

Vial temperature: The vials are maintained at a temperature of 80° for 45 min before headspace injection.

System suitability

Sample: *Standard solution B*

Suitability requirements

Relative standard deviation: NMT 15% from 3 injection

Analysis

Samples: ▲▲ (ERR 1-Jun-2021) *Standard solution A*, *Standard solution B*, *Standard solution C*, and *Sample solution*

The detector response factor (*RF*) of each *Standard solution* is determined by:

$$RF = (W_{SS} \times C_{SS})/(r_S - r_U)$$

W_{SS} = weight of the *Standard stock solution* in each *Standard solution* (g)

C_{SS} = concentration of benzene in the *Standard stock solution* (µg/g)

r_S = peak area of benzene in each *Standard solution*

r_U = peak area of benzene in the *Sample solution*

Average three *RF* to obtain RF_{avg}. Calculate the percentage of benzene in the portion of Carbomer Copolymer taken:

$$\text{Result} = [(RF_{avg} \times r_U)/W_U] \times 100$$

RF_{avg} = average of three *RF*

r_U = peak area of benzene in the *Sample solution*

W_U = weight of Carbomer Copolymer in the *Sample solution* (µg)

Acceptance criteria: NMT 0.0002%, corresponding toNMT 2 µg/g

• **Limit of Acrylic Acid**

Solution A: Methanol

Solution B: Dissolve 6.80 g of monobasic potassium phosphate in 300 mL of water, dilute with water to 500 mL. Dilute 100 mL of this solution with water to 1 L, adjust with phosphoric acid to a pH of 3.0 ± 0.1. Filter and degas.

Mobile phase: See *Table 3*.

Table 3

Time (min)	Solution A (%)	Solution B (%)	Flow Rate (mL/min)
0	5	95	1.0
8	5	95	1.0
9	10	90	1.5
19	10	90	1.5
20	5	95	1.0
25	5	95	1.0

Standard solution A: 2 µg/g of acrylic acid (w/w)

Standard solution B: 50 µg/g of acrylic acid (w/w)

Standard solution C: 100 µg/g of acrylic acid (w/w)

Sample solution: Transfer 100 mg of Carbomer Copolymer to a tared serum vial. Add water to obtain a total weight of 10 g of solution. Cap the vial, and shake by mechanical means for 2 h. Add 2 drops of sodium hydroxide solution (50% w/v), and shake by hand for 15 s. Add 1.0 mL of calcium chloride solution (100 mg/mL), and shake until the gel collapses. Record the weight of all additions of water, sodium hydroxide, and calcium chloride. Centrifuge for 15 min, and use the clear supernatant.

Chromatographic system

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

Mode: LC

Detector: UV 200 nm

Column: 4.6-mm × 15-cm; 5 µm packing L1

Flow rate: See *Table 3*.

Injection volume: 10 µL

System suitability

Sample: *Standard solution B*

Suitability requirements

Relative standard deviation: NMT 5% from 3 injections

Analysis

Samples: *Standard solution A*, *Standard solution B*, *Standard solution C*, and *Sample solution*

Analyze each *Standard solution*, and plot the peak area versus concentration. Plot should be linear with an r^2 equal or greater than 0.9990. The slope of the calibration curve (area/ppm acrylic acid) is the response factor. Calculate the percentage of free acrylic acid in the portion of Carbomer Copolymer taken:

$$\text{Result (wt\%)} = (r_U/RF)/C_U \times F \times 100$$

r_U = peak response of acrylic acid from the *Sample solution*

RF = response factor [peak area/(µg/g)]

C_U = concentration of Carbomer Copolymer in the *Sample solution* (mg/g)

F = unit conversion factor, 10^{-3} (mg/µg)

Acceptance criteria: NMT 0.25%

SPECIFIC TESTS

- **Loss on Drying ⟨731⟩**

Analysis: Dry under vacuum at 80° for 1 h.

Acceptance criteria: NMT 2.0%

- **Viscosity—Rotational Methods ⟨912⟩**

Sample: 5.00 g of Carbomer Copolymer, previously dried under vacuum at 80° for 1 h

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Direct titration

Electrode: Calomel–glass or silver/silver chloride

Titrant: 180 mg/mL of sodium hydroxide

Endpoint detection: pH

Analysis: Carefully add the *Sample* to 500 mL of water in an 800-mL beaker,[1] while stirring continuously at 1000 ± 10 rpm, with the stirrer shaft set to one side of the beaker at an angle of 60° and the propeller positioned near the bottom of the beaker. Allow 45–90 s for addition of the *Sample* at a uniform rate, being sure that loose aggregates of powder are broken up, and continue stirring at 1000 ± 10 rpm for 15 min. [Note—Proper dispersion of the carbomer resin is imperative for accurate viscosity readings.] Remove the stirrer, and place the beaker containing the dispersion in a 25 ± 0.1° water bath for 30 min. Insert a paddle stirrer to a depth necessary to ensure that air is not drawn into the dispersion; and while stirring at 300 ± 25 rpm, titrate with *Titrant* to a pH of 7.3–7.8. Stir 2–3 min until neutralization is complete. [Note—After neutralization, care must be taken to avoid excessively high shearing, because aggressive mixing will break the polymer chains and reduce the viscosity reading.] Then determine the final pH. [Note—If the pH is below 7.3, raise it with additional *Titrant*. If it is above 7.8, discard the mucilage, and prepare another batch, using a smaller amount of *Titrant* for titration.]

Return the beaker containing the neutralized mucilage to the 25 ± 0.1° water bath for 1 h. Equip a suitable rotational viscometer [2] with a suitable spindle as defined in *Table 4*. The spindle rotates at 20 rpm. Follow the instrument manufacturer's directions to measure the apparent viscosity.Perform the viscosity determination without delay to avoid the slight viscosity changes that occur 75 min after neutralization.

Table 4

Viscosity Ranges (mPa · s)	Spindle No.	A[a] (cm)	B[b] (cm)	C[c] (cm)	D[d] (cm)	E[e] (cm)	Multiplier
100–400	1	5.6	2.2	0.3	2.7	6.1	5
400–1,600	2	4.7	0.2	0.3	2.7	4.9	20
1,000–4,000	3	3.5	0.2	0.3	2.7	4.9	50
2,000–8,000	4	2.7	0.2	0.3	2.7	4.9	100
4,000–16,000	5	2.1	0.2	0.3	2.7	4.9	200

Viscosity Ranges (mPa · s)	Spindle No.	A[a] (cm)	B[b] (cm)	C[c] (cm)	D[d] (cm)	E[e] (cm)	Multiplier
10,000–40,000	6	1.5	0.2	0.3	3.0	4.9	500
40,000–160,000	7	—	—	0.3	—	5.5	2,000

[a] Cylinder diameter.

[b] Cylinder height.

[c] Shaft diameter.

[d] Distance from the top of the cylinder to the lower tip of the shaft.

[e] Spindle immersion depth.

Acceptance criteria: See *Table 5*.

Table 5

Carbomer Copolymer	1% Viscosity Specification (mPa · s)
A	4,500–13,500
B	14,000–26,500
C	27,000–45,000

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Product is hygroscopic. Preserve in tight containers away from direct sources of moisture.

• **Labeling:** If benzene has been used in the manufacturing process, the name of the article will be Carbomer 1342, provided it complies with and is labeled in accordance with the requirements set forth in that monograph. If benzene is not used in the manufacturing process, label it to indicate whether it is Type A, B, or C; and label it to state the measured viscosity, giving the viscosity measurement parameters, the concentration of the solution, and the type of equipment used; the solvent or solvents used in the polymerization process; and the nominal and residual solvent levels for each solvent.

• **USP Reference Standards** ⟨11⟩
USP Carbomer Copolymer RS

[1] A beaker size of 600–1000 mL is ideal for this method. However, the minimum inside diameter of the beaker should be 83 mm.

[2] Available as a Brookfield RV viscometer, or equivalent.

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

Topic/Question	Contact	Expert Committee
CARBOMER COPOLYMER	Documentary Standards Support	CE2020 Complex Excipients

Chromatographic Database Information: Chromatographic Database

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