

Residual Ethyl Acetate and Cyclohexane

Applicable Products: Carbopol[®]* Polymers, Pemulen[™]* Polymeric Emulsifiers and Noveon[®]* AA-1 Polycarbophil

Scope:

This procedure is for the analysis of residual solvent levels in Carbopol[®] polymers, Pemulen[™] polymeric emulsifiers or Noveon[®] AA-1 polycarbophil polymerized in ethyl acetate or ethyl acetate/cyclohexane mixtures.

Abstract:

The residual solvents are extracted from a sample of the polymer by shaking with methanol. A 2 µl sample of the extract is injected onto a gas chromatograph column and the components separated. The responses of the solvent peaks are compared to the responses of prepared standards to determine the concentrations. Methyl ethyl ketone (MEK) is added to all samples and standards as an internal standard.

Safety Precautions:

1. Wear safety goggles and gloves and follow good laboratory practices.
2. Polymer dust is irritating to the respiratory passages and breathing it should be avoided.
3. Methanol, ethyl acetate, cyclohexane and methyl ethyl ketone (MEK) are all flammable and should be handled accordingly.
4. See all Material Safety Data Sheets (MSDS) for additional safety and handling information.

Interferences:

While no interferences have been recognized, any unknown component eluting at the same retention time as ethyl acetate, cyclohexane or

the internal standard, methyl ethyl ketone, would influence the results. These interferences could be present in the polymer or the methanol used to extract.

Apparatus:

1. Gas chromatograph equipped with a packed column inlet and flame ionization detector.
2. Data processing station.
3. 10' x 1/4" glass column packed with 1% SP-1000 on Carbopack B (60/80 mesh) – (see Special Instruction 1 for column preparation instructions).
4. Mechanical shaker.
5. 30 mL serum bottle.
6. 10 mL serum bottle.
7. Serum bottle rubber stopper.
8. Aluminum seals for serum bottles.
9. Manual aluminum seal crimper.
10. Automatic burette, Brinkmann Digital, 25 mL (for methanol addition).
11. Hamilton syringe, 10 ul.
12. Hamilton syringe, 50 ul.
13. Analytical balance capable of ±0.0001 gram accuracy.

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Reagents:

1. Methanol, ACS certified.
2. Ethyl acetate, ACS certified.
3. Methyl ethyl ketone, ACS certified.
4. Cyclohexane, ACS certified.

GC Conditions:

Detector temperature	250°C.
Injection port temperature	250°C.
Helium flow rate	33 cc/min
Hydrogen flow rate	50 cc/min
Air flow to flame	330 cc/min
Oven conditions	
Initial temperature	115°C.
Initial time	4 minutes
Ramp rate	6 deg/minute
Final temperature	175°C.
Final time	5 minutes

Calibration:

Primary Standard

1. Accurately weigh a 10 mL serum bottle with rubber stopper. (All weights are to four decimal places.)
2. Add 5 mL methanol and insert the rubber stopper and reweigh.
3. Add 50 µl ethyl acetate through the rubber stopper and reweigh.
4. Add 50 µl cyclohexane through the rubber stopper and reweigh.
5. Mix thoroughly.

Working Standard

6. Accurately weigh a 30 mL serum bottle with rubber stopper.
7. Add 20 mL methanol, insert the rubber stopper and reweigh.
8. Add 10 µl methyl ethyl ketone through the rubber stopper and reweigh.
9. Add 50 µl of the Primary Standard through the rubber stopper and reweigh. This is the Working Standard.
10. Inject 2 µl of the Working Standard onto the gas chromatograph column and analyze using the conditions noted in the GC Conditions section.
11. A calibration file can be established with the data processing station.

Procedure:

1. Weigh a 30 mL serum vial with a septum and record the weight (all weights are to four decimal places).
2. Add 50 mg (0.05 gram) of the polymer to the vial and reweigh. The sample size is not critical and sample weights of 0.04 to 0.06 gram are acceptable.
3. Using the automatic burette, dispense 20 mL of methanol to the vial, rubber stopper and reweigh.
4. Add 10 µl MEK through the rubber stopper and record the weight. (The weight of 10 µl MEK is appropriately 0.0077 gram.) If the internal standard amount is significantly different, discard and begin preparation of another sample.
5. Place on the mechanical shaker for one half hour of vigorous shaking to extract the ethyl acetate and cyclohexane into the methanol.
6. Determine that the gas chromatograph is ready for the analysis. The operating conditions listed in the GC Conditions section should be entered.
7. Inject 2 µl of sample onto the gas chromatograph column.
8. Run time is 19 minutes.

Calculations:

No calculations are necessary if the data system is calibrated.

In the event automated peak detection and measurement are not used, the following calculations will yield the percent ethyl acetate and cyclohexane:

A. Calculation of response factor (RF) for ethyl acetate

$$\frac{WTE}{WTT} \times \frac{WT \text{ P.S.}}{0.05} \times 100 = \text{WT\% ETAC in 0.05 g polymer}$$

Where WTE = weight of ethyl acetate in Primary Standard
WTT = total of weight of Primary Standard
WT PS = weight of PS in Secondary Standard

$$RF = \frac{AREA \text{ IS}}{AREA \text{ E}} \times \frac{WT\% \text{ ETAC}}{WT \text{ IS}/.0005}$$

Where Area IS = area of Internal Standard peak
Area E = area of ethyl acetate peak
WT% ETAC = value from step 1 above
WT IS = weight of Internal Standard in Working Standard

Example:

$$\text{WT\% ETAC} = \frac{0.0505}{3.9832} \times \frac{0.0444}{0.05} \times 100$$

$$\text{WT\% ETAC} = 1.1258$$

$$\text{RF} = \frac{6867}{317} \times \frac{1.1258}{.0080/.0005}$$

$$\text{RF} = 1.5242$$

B. Calculation of weight percent ethyl acetate in sample is calculated as follows:

$$\text{WT\% ETAC} = \text{RF} \times \frac{\text{AREA E2} \times \text{WT IS2}}{\text{AREA IS2} \times \text{WT S}} \times 100$$

Where RF = response factor for ethyl acetate from calculation in A
AREA E2 = area ETAC in sample
AREA IS2 = area Internal Standard in sample
WT IS2 = weight Internal Standard in sample
WT S = weight of sample

Example:

$$\text{WT\% ETAC} = 1.5242 \times \frac{87}{6902} \times \frac{.0083}{.0564} \times 100$$

$$\text{WT\% ETAC} = 0.28$$

C. Repeat calculations for cyclohexane

Special Instructions:

1. The 10' x 1/4" column packed with 1% SP-1000 on Carbopack B (60/80 mesh) is custom packed by Supelco (see Apparatus section). The column should be conditioned prior to its initial use. Connect the column to the gas chromatograph inlet only. Do not connect to the detector until conditioning is completed. Set the carrier gas flow to 33 cc/min and the oven temperature to 175°C. The column should be ready for use after a 24 hours conditioning period.

References:

- *Current edition of the United States Pharmacopeia/National Formulary (USP/NF)*