

Application News

Gas Chromatograph HS-20 NX USTL/Brevis™ GC-2050

Efficient Analysis of Residual Solvents in Pharmaceuticals Using the Compact Model, Brevis GC-2050 (1)

—JP18 and USP467, Water-Soluble Samples—

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User Benefits

- The slim and compact design of the Brevis GC-2050 enables the expansion of the number of operational units in the laboratory, allowing for efficient high-throughput analysis.
- Brevis GC-2050 can perform analysis using alternative carrier gases.
- Analysis can be performed with tert-butyl alcohol and cyclopentyl methyl ether, which have been newly added as Class 2 solvents in ICH Q3C (R8).

■ Introduction

Residual solvents in pharmaceuticals are defined as organic volatile chemical substances that are used or produced in the manufacture of drug substances or additives or in the preparation of drug products. In the Japanese Pharmacopoeia 18th Edition (JP18) or the United States Pharmacopeia (USP) General Chapters <467> Residual Solvents, residual solvents are classified as Class 1 to 3, according to their risk to human health, and the headspace GC method is mainly used to analyze them. The carrier gas that is normally used is He. However, He supply shortages have become an issue recently, so there is a demand to perform analysis using alternative carrier gases, such as H₂ or N₂.

This article introduces the results of analysis of Class 1 and 2 water-soluble samples using the compact design Brevis GC-2050. For the Procedure A, H₂ and N₂ in addition to He were used. When using an alternative carrier gas, it is necessary to first verify the operation based on USP General Chapter < 1467>.

■ Instrument Configuration and Analytical **Conditions**

Table 1 Analytical Conditions of Water-Soluble Samples

GC Analytical Conditions (Procedure A and B) : Brevis GC-2050 Model

Detector : FID (Flame Ionization Detector)

A) SH-I-624Sil MS Column

 $(0.32 \text{ mm I.D.} \times 30 \text{ m, d.f.} = 1.8 \mu\text{m})$

B) SH-PolarWax

(0.32 mm l.D. \times 30 m, d.f. = 0.25 μ m)

Column Temp. A) 40 °C (20 min) – 10 °C/min – 240 °C (20 min)

Total 60 mins

B) 50 °C (20 min) - 6 °C/min - 165 °C (20 min)

Total 59.17 mins

Injection Mode A) Split 1:5

B) Split 1:10

Linear velocity (He, N₂, H₂) Carrier Gas Controller

Linear Velocity 35 cm/sec Detector Temp. 250 °C FID H₂ Flowrate 32 mL/min FID Makeup Flowrate 24 mL/min (N₂) FID Air Flowrate 200 mL/min Injection Volume 1 mL

HS-20 NX Analytical Conditions (Same for Procedure A and B)

: HS-20 NX USTL (Ultra Short Transfer Line) Model

Oven Temp 80 °C Sample Line Temp. 110 °C Transfer Line Temp. : 120 °C Vial Shaking Level Off Vial Volume 20 mL Vial Equilibrating Time: 60 min Vial Pressurizing Time 1 min Vial Pressure 75 kPa Loading Time 0.5 min Load Equilib. Time 0 min Needle Flush Time : 5 min



Fig. 1 HS-20 NX USTL (Ultra Short Transfer Line) + Brevis™ GC-2050

■ Class 1 Standard Solution Analysis (Water-**Soluble Samples)**

Figs. 2 and 3 show the analysis results for the Class 1 standard solution.

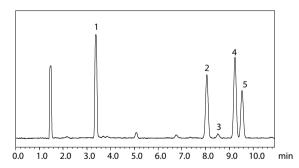


Fig. 2 Class 1 Standard Solution Chromatogram (Water-Soluble Sample) Using Procedure A

1. 1.1-Dichloroethane. 2. 1.1.1-Trichloroethane.

5. 1.2-Dichloroethane 3. Carbon tetrachloride. 4. Benzene.

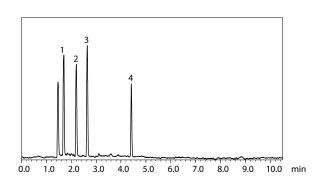


Fig. 3 Class 1 Standard Solution Chromatogram (Water-Soluble Sample) Using Procedure B

1. 1,1-Dichloroethane,

2. 1,1,1-Trichloroethane+ Carbon tetrachloride,

3. Benzene, 4. 1,2-Dichloroethane

■ Class 2 Standard Solution Analysis (Water-Soluble Samples)

Fig. 4 shows the analysis results for Procedure A, and Fig. 5 shows the analysis results for Procedure B (Class 2A: black, Class 2B: pink, TBA, CPME, MiBK: blue). For system suitability, JP18 specifies that "the resolution between acetonitrile and methylene chloride in the Class 2 mixture A standard solution is not less than 1.0" when using Procedure A, and "the resolution between acetonitrile and cis-1,2-dichloroethene in the Class 2 mixture A standard solution is not less than 1.0" when using Procedure B. Satisfactory results were obtained with both procedures.

Note: The resolutions shown in the Figs. 4 and 5 are reference values and not guaranteed.

Note: A mixture of standard samples of *tert*-butyl alcohol (TBA), cyclopentyl methyl ether (CPME), and methyl isobutyl ketone (MiBK) was separately prepared to the prescribed concentration.

■ Analysis of Class 1 and 2 Standard Samples (Water-Soluble Samples) by Procedure A Using H₂ or N₂ Carrier Gas

Figs. 6 to 9 show the separation patterns for Procedure A using the alternative gases $\rm H_2$ and $\rm N_2$. When using an alternative carrier gas, the system suitability should be checked before performing the operation.

■ Conclusion

Even though the Brevis GC-2050 is small and compact, it is capable of analyzing residual solvents in pharmaceuticals in accordance with the JP18 and USP General Chapters <467> Residual Solvents. That compactness means the number of units installed in a laboratory can be increased compared with high-end models, so residual solvents in pharmaceuticals can be efficiently analyzed.

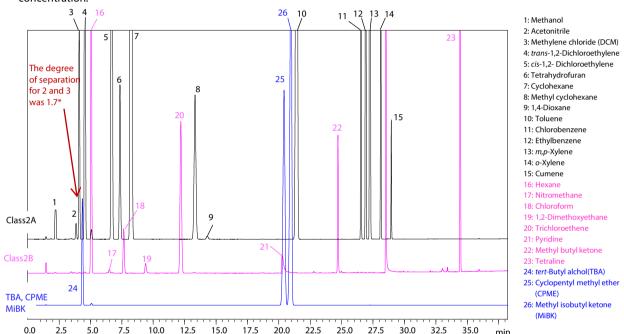


Fig. 4 Class 2 Standard Solution Chromatogram (Water-Soluble Sample) Using Procedure A

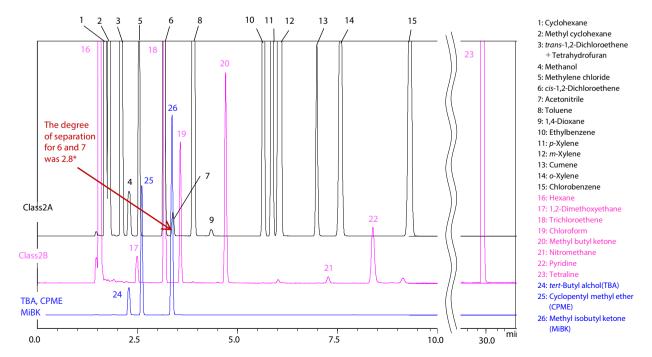


Fig. 5 Class 2 Standard Solution Chromatogram (Water-Soluble Sample) Using Procedure B

■ Examples of Analysis of Class 1 and 2 Standard Samples (Water-Soluble Samples) Using an **Alternative Carrier Gas**

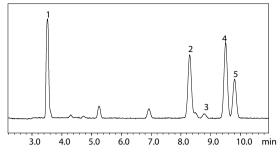


Fig. 6 Class 1 Standard Solution Chromatogram (Water-Soluble Sample) by Procedure A Using N2 Carrier Gas

- 1,1-Dichloroethane, 2. 1,1,1-Trichloroethane,
- 3. Carbon tetrachloride, 4. Benzene,
- 5. 1,2-Dichloroethane

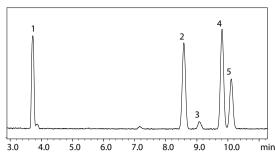
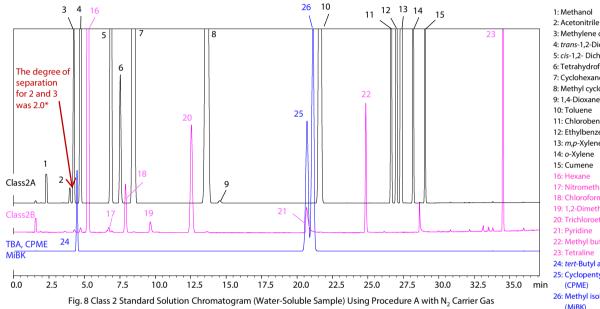


Fig. 7 Class 1 Standard Solution Chromatogram (Water-Soluble Sample) by Procedure A Using H2 Carrier Gas

- 1. 1,1-Dichloroethane, 2. 1,1,1-Trichloroethane,
- 3. Carbon tetrachloride, 4. Benzene, 5. 1,2-Dichloroethane



10 26 13 14 The degree of 25 separation for 2 and 3 was 2.1* Class2B 24 ТВА, СРМЕ 5.0 7.5 10.0 17.5 20.0 22.5 25.0 27.5 0.0 2.5 12.5 15.0 30.0 32.5 35.0 Fig. 9 Class 2 Standard Solution Chromatogram (Water-Soluble Sample) Using Procedure A with H₂ Carrier Gas * The Class 2A reagent used in the H $_{2}$ carrier gas analysis shown in Fig. 9 included MiBK.

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1: Methanol

3: Methylene chloride (DCM)

4: trans-1,2-Dichloroethylene 5: cis-1,2- Dichloroethylene

6: Tetrahydrofuran

7: Cyclohexane

8: Methyl cyclohexane

9: 1,4-Dioxane

10: Toluene 11: Chlorobenzene

12: Ethylbenzene

13: m.p-Xvlene

14: o-Xvlene

15: Cumene

17: Nitromethane

18: Chloroform

19: 1,2-Dimethoxyethane

20: Trichloroethene

21: Pyridine

22: Methyl butyl ketone

24: tert-Butyl alchol(TBA)

25: Cyclopentyl methyl ether (CPMF)

26: Methyl isobutyl ketone (MiBK)

1: Methanol

2: Acetonitrile

3: Methylene chloride (DCM)

4: trans-1,2-Dichloroethylene

5: cis-1,2- Dichloroethylene

6: Tetrahydrofuran

7: Cyclohexane

8: Methyl cyclohexane

9· 1 4-Dioxane

10: Toluene

11: Chlorobenzene 12: Ethylbenzene

13: m.p-Xvlene

14: o-Xvlene

15: Cumene

17: Nitromethane

18: Chloroform

19: 1,2-Dimethoxyethane 20: Trichloroethene

21: Pyridine

22: Methyl butyl ketone

23: Tetralin

24: tert-Butyl alchol(TBA) 25: Cyclopentyl methyl ether

(CPME) 26: Methyl isobutyl ketone

(MiBK)

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