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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 H_2 or N_2.

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, H_2 and N_2 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>.

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

■ Instrument Configuration and Analytical Conditions

Table 1 Analytical Conditions of Water-Soluble Samples

GC Analytical Conditions (Procedure A and B)	
Model	: Brevis GC-2050
Detector	: FID (Flame Ionization Detector)
Column	: A) SH-I-624Sil MS (0.32 mm I.D. × 30 m, d.f. = 1.8 µm) B) SH-PolarWax (0.32 mm I.D. × 30 m, d.f. = 0.25 µm)
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
Carrier Gas Controller	: Linear velocity (He, N_2, H_2)
Linear Velocity	: 35 cm/sec
Detector Temp.	: 250 °C
FID H_2 Flowrate	: 32 mL/min
FID Makeup Flowrate	: 24 mL/min (N_2)
FID Air Flowrate	: 200 mL/min
Injection Volume	: 1 mL
HS-20 NX Analytical Conditions (Same for Procedure A and B)	
Model	: HS-20 NX USTL (Ultra Short Transfer Line)
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

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

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

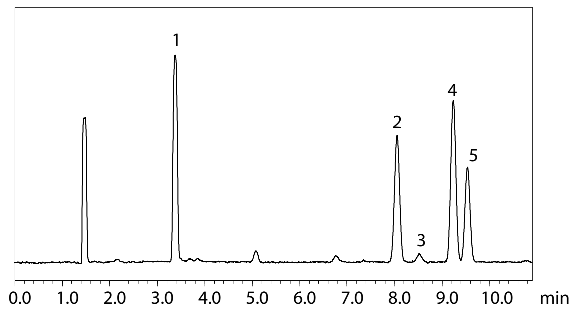


Fig. 2 Class 1 Standard Solution Chromatogram (Water-Soluble Sample) Using Procedure A

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

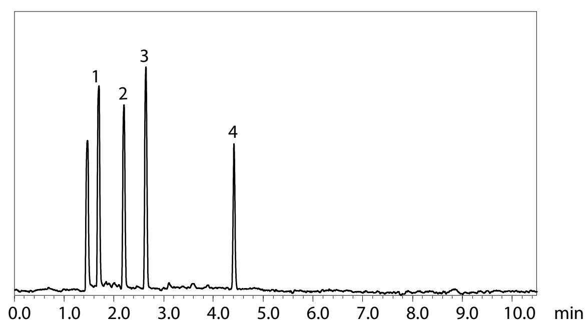


Fig. 3 Class 1 Standard Solution Chromatogram (Water-Soluble Sample) Using Procedure B

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 H_2 or N_2 Carrier Gas

Figs. 6 to 9 show the separation patterns for Procedure A using the alternative gases H_2 and 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.

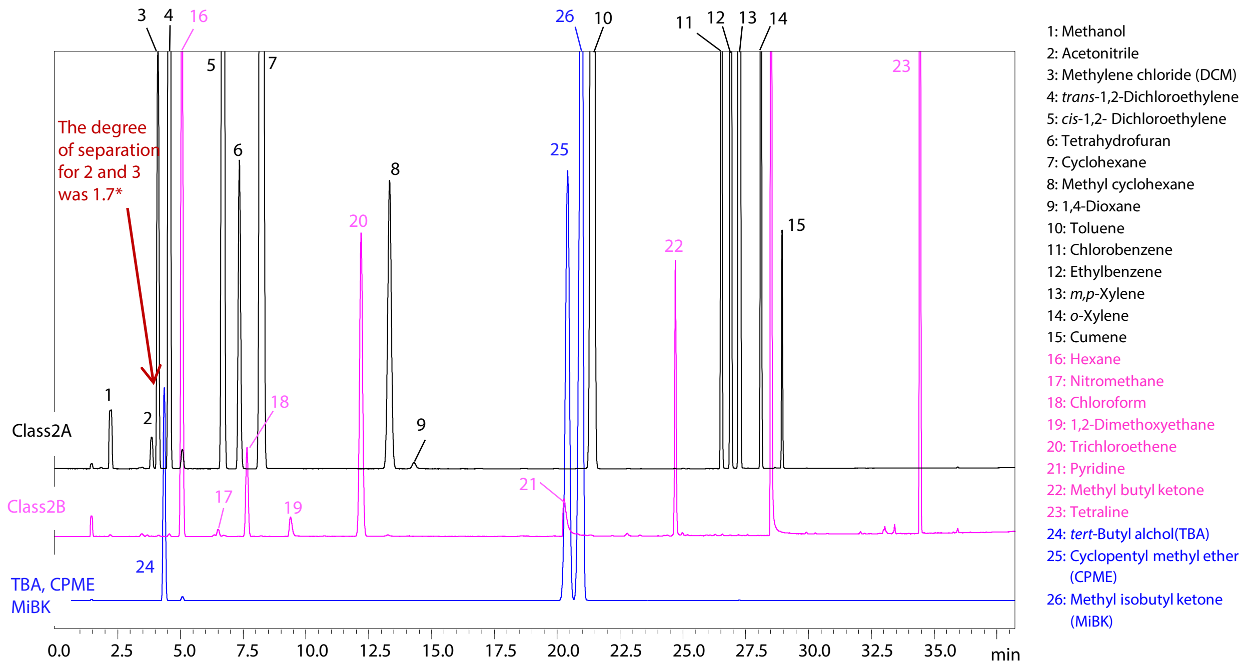


Fig. 4 Class 2 Standard Solution Chromatogram (Water-Soluble Sample) Using Procedure A

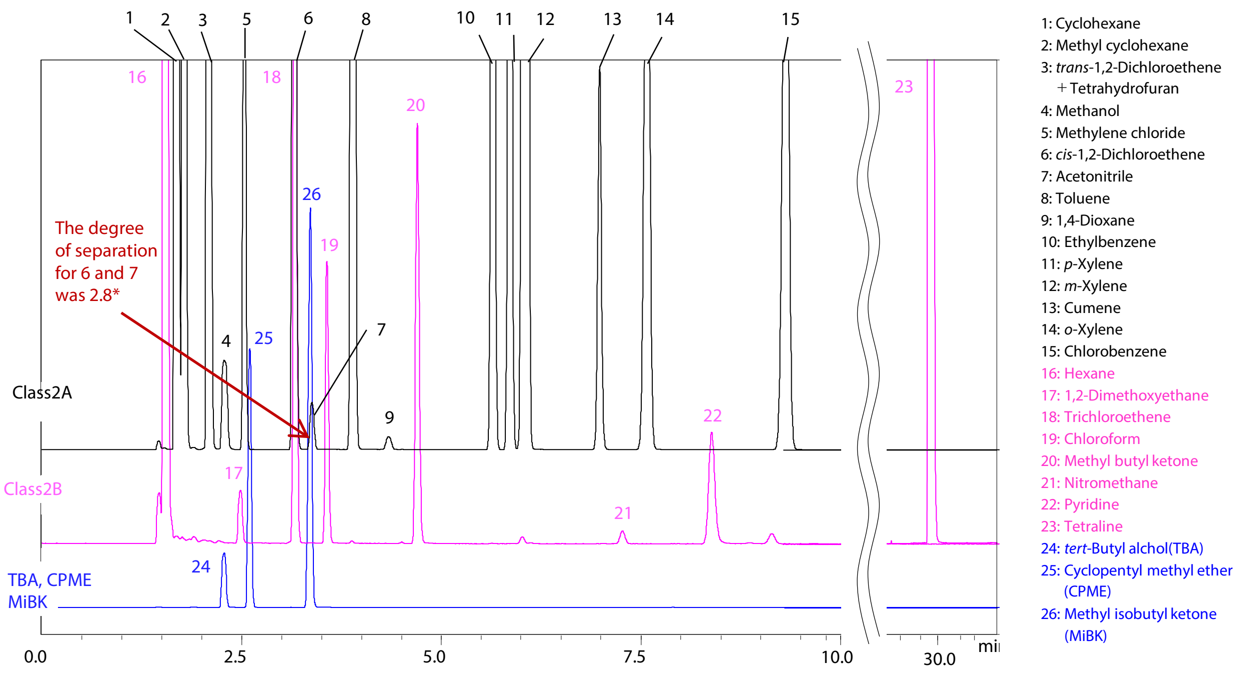


Fig. 5 Class 2 Standard Solution Chromatogram (Water-Soluble Sample) Using Procedure B

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

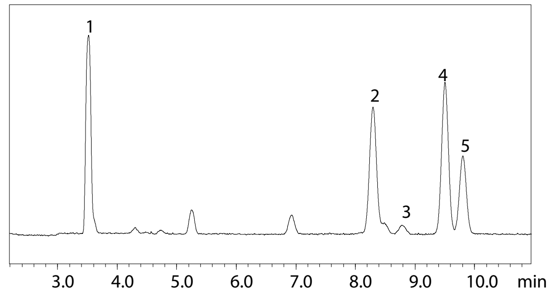


Fig. 6 Class 1 Standard Solution Chromatogram (Water-Soluble Sample) by Procedure A Using N_2 Carrier Gas

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

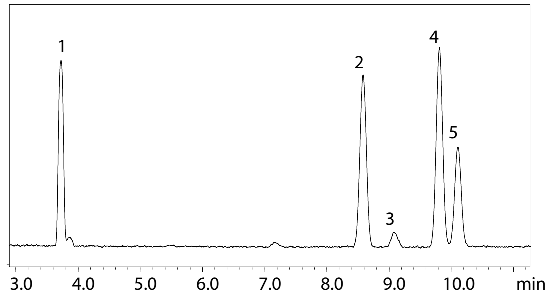
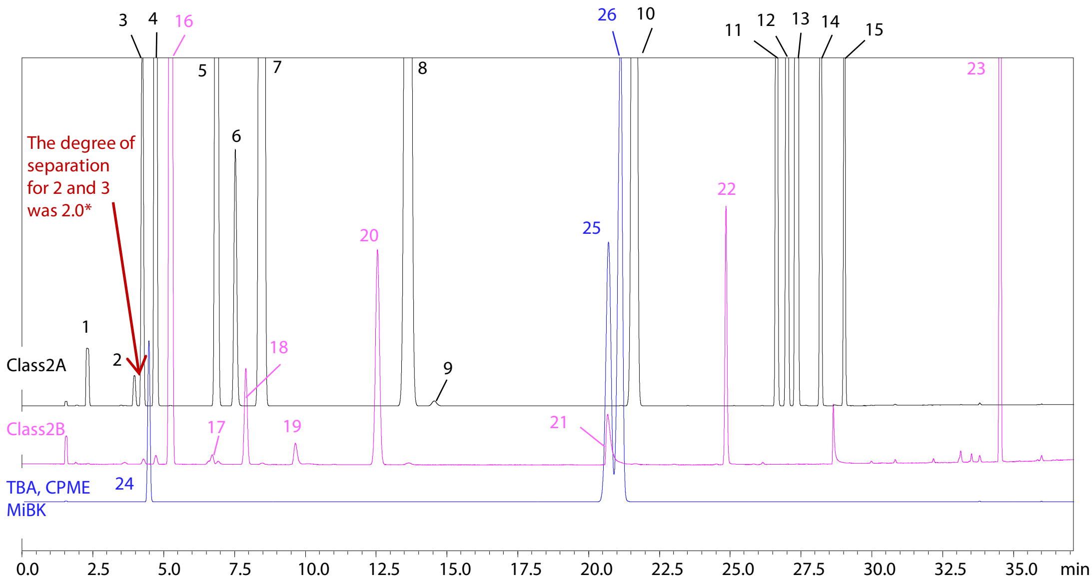


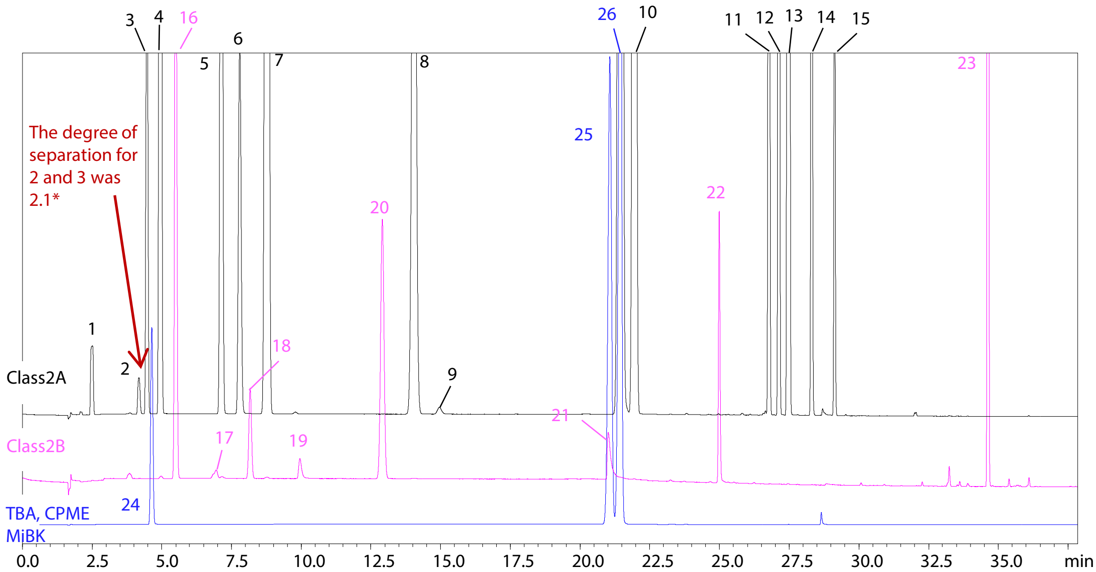
Fig. 7 Class 1 Standard Solution Chromatogram (Water-Soluble Sample) by Procedure A Using H_2 Carrier Gas

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



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*-Xylene
14: *o*-Xylene
15: Cumene
16: Hexane
17: Nitromethane
18: Chloroform
19: 1,2-Dimethoxyethane
20: Trichloroethene
21: Pyridine
22: Methyl butyl ketone
23: Tetraline
24: *tert*-Butyl alchol(TBA)
25: Cyclopentyl methyl ether (CPME)
26: Methyl isobutyl ketone (MiBK)

Fig. 8 Class 2 Standard Solution Chromatogram (Water-Soluble Sample) Using Procedure A with N_2 Carrier Gas



1: Methanol
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6: Tetrahydrofuran
7: Cyclohexane
8: Methyl cyclohexane
9: 1,4-Dioxane
10: Toluene
11: Chlorobenzene
12: Ethylbenzene
13: *m,p*-Xylene
14: *o*-Xylene
15: Cumene
16: Hexane
17: Nitromethane
18: Chloroform
19: 1,2-Dimethoxyethane
20: Trichloroethene
21: Pyridine
22: Methyl butyl ketone
23: Tetraline
24: *tert*-Butyl alchol(TBA)
25: Cyclopentyl methyl ether (CPME)
26: Methyl isobutyl ketone (MiBK)

Fig. 9 Class 2 Standard Solution Chromatogram (Water-Soluble Sample) Using Procedure A with H_2 Carrier Gas

* The Class 2A reagent used in the H_2 carrier gas analysis shown in Fig. 9 included MiBK.

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