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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 (2) —JP18 and USP467, Water Insoluble 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 comply with the analysis methods of the pharmacopoeias.
- Analysis can be performed on *tert*-butyl alcohol and cyclopentyl methyl ether, which have been newly added as Class 2 solvents in ICH Q3C (R8).

■ Introduction

The methods of testing for residual solvents in pharmaceuticals are strictly prescribed in the Japanese Pharmacopoeia 18th Edition (JP18) and the United States Pharmacopeia (USP) General Chapters <467> Residual Solvents. In order to efficiently perform tests for residual solvents in pharmaceuticals under prescribed test methods, it is important to increase the number of instruments installed in laboratories, which often have limited space. The Brevis GC-2050 (Fig. 1) has a compact design, and compared with existing GC, the width of the system can be reduced by about 35 %. In addition, headspace samplers with ultra-short transfer lines can be used to further increase the number of units in the lab and enhance analysis efficiency. This article introduces the results of analysis of Class 1 and 2 water-insoluble samples using the compact Brevis GC-2050, in accordance with Supplement 2 of the JP18. DMF was used as the solvent.

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

■ Analytical Conditions

Table 1 Analysis Conditions of Water-Insoluble Sample

GC Analytical Conditions (Procedure A and B)		
Model	:	Brevis GC-2050
Detector	:	FID (Flame Ionization Detector)
Column	:	A) SH-I-624Sil MS (0.53 mm I.D. × 30m, d.f. = 3.0 µm) B) SH-PolarWax (0.32 mm I.D. × 30m, 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 GC Analytical Conditions (Same for Procedure A and B)		
Model	:	HS-20 NX USTL (Ultra Short Transfer Line)
Oven Temp.	:	80 °C
Sample Line Temp.	:	90 °C
Transfer Line Temp.	:	105 °C
Vial Shaking Level	:	Off
Vial Volume	:	20 mL
Vial Equilibrating Time	:	45 min
Vial Pressurizing Time	:	1 min
Vial Pressure	:	68.9 kPa
Loading Time	:	0.5 min
Load Equilib. Time	:	0 min
Needle Flush Time	:	5 min

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

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

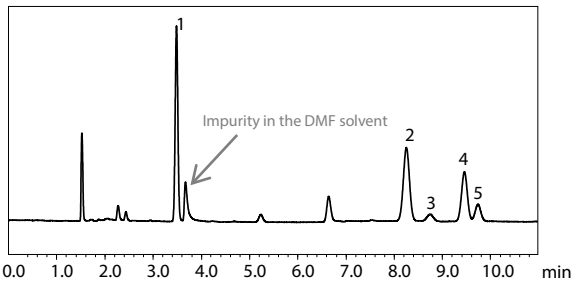

Fig. 2 Class 1 Standard Solution Chromatogram (Water-Insoluble Sample) Using Procedure A
1. 1,1-Dichloroethane, 2. 1,1,1-Trichloroethane,
3. Carbon tetrachloride, 4. Benzene, 5. 1,2-Dichloroethane

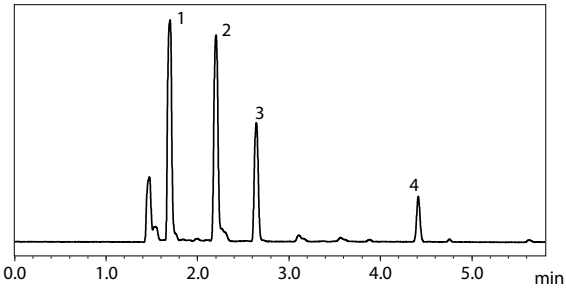

Fig. 3 Class 1 Standard Solution Chromatogram (Water-Insoluble Sample) Using Procedure B
1. 1,1-Dichloroethane, 2. 1,1,1-Trichloroethane+ Carbon tetrachloride,
3. Benzene, 4. 1,2-Dichloroethane

■ Class 2 Standard Solution Analysis (Water-Insoluble Sample)

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.

■ 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.

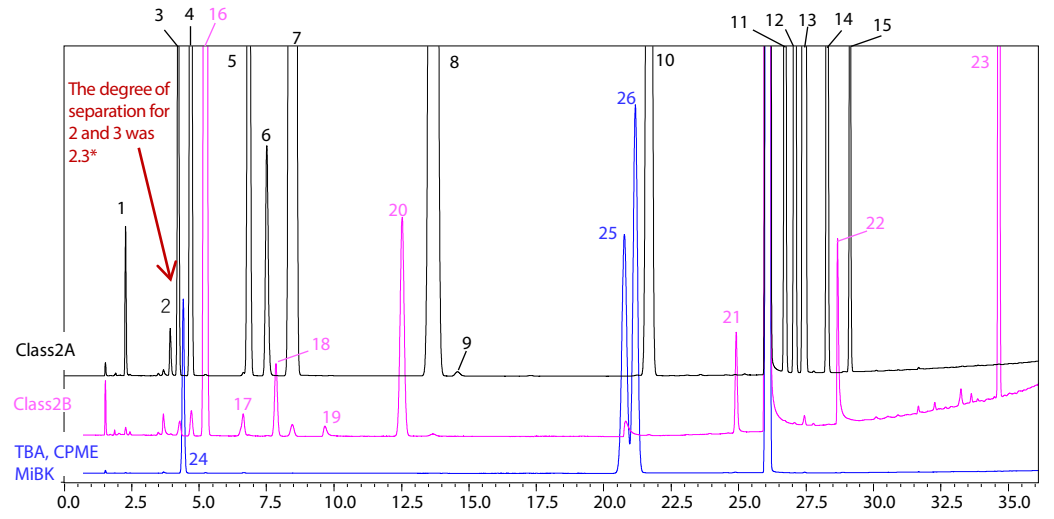

Fig. 4 Class 2 Standard Solution Chromatogram (Water-Insoluble Sample) Using Procedure A

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 alcohol (TBA)
25: Cyclopentyl methyl ether (CPME)
26: Methyl isobutyl ketone (MiBK)

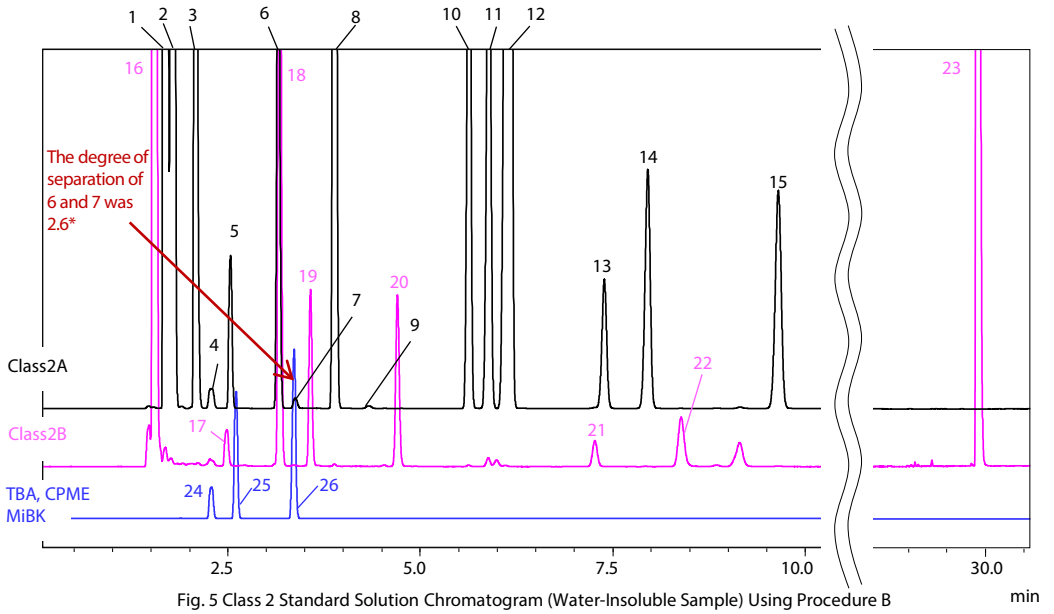

Fig. 5 Class 2 Standard Solution Chromatogram (Water-Insoluble Sample) Using Procedure B

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

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