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Application News

GC HS-20 NX/Nexis™ GC-2030

Analysis of Residual Solvents in Pharmaceuticals by Water-Soluble Samples Using H_2 Carrier (USP 467)

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User Benefits

- The use of H_2 as a carrier gas, which is inexpensive and easy to obtain, contributes to cost reduction in the laboratory.
- H_2 carrier gas is used to achieve the accuracy required by the USP.
- A hydrogen sensor ensures H_2 carrier gas can be used safely.
- Using a state-of-the-art HS-20 NX headspace sampler enables reliable measurement of residual solvents in pharmaceuticals.

■ Introduction

Test methods for residual solvents in pharmaceuticals are specified in the USP (United States Pharmacopeia) General Chapter <467> Residual Solvents, which mainly specifies using the headspace GC method. Residual solvents in pharmaceuticals are classified into Classes 1 to 3 based on potential risks to human health and strictly controlled accordingly. Sensitive analysis is required. The carrier gas generally used for analysis is He, but the depletion of He has become a problem recently. Consequently, there is a need for using an alternative carrier gas such as H_2 for analysis. Any method changes, such as substituting He with an alternate carrier gas, must be validated according to USP Chapter <1467> Residual Solvents—Verification of Compendial Procedures and Validation of Alternative Procedures.

This paper presents the results of using H_2 as a carrier gas with an HS-20 NX headspace sampler to analyze Class 1 and 2 water-soluble samples in accordance with USP General Chapter <467> Residual Solvents.

* Analytical samples were prepared using a different procedure from the USP to confirm the performance of the apparatus.

■ Instrument Configuration and Analysis Conditions

A Nexis GC -2030 gas chromatograph and Shimadzu HS-20 NX headspace gas sampler were connected to measure the listed Class 1 and Class 2 standard solutions according to USP General Chapter <467> Residual Solvents, Procedure A. The analytical conditions for GC and HS are indicated in Table 1.

Table 1 Water-Soluble Sample Analysis Conditions

GC Analysis Conditions (Procedure A)	
Model:	Nexis GC-2030
Detector:	FID-2030 flame ionization detector
Column:	SH-I-624Sil MS (0.32 mm I.D.×30 m, d.f.= 1.8 µm) *1
Column Temp.:	40 °C (20 min) – 10 °C/min – 240 °C (20 min) Total 60 min
Injection Mode:	Split 1:5
Carrier Gas Controller:	Constant linear velocity mode (H_2 and He)
Linear Velocity:	35 cm/sec
Detector temp.:	250 °C
FID H_2 Flowrate:	32 mL/min
FID Make-up Flowrate:	24 mL/min (N_2)
FID Air Flowrate:	200 mL/min
HS Analysis Conditions (Procedure A)	
Oven Temperature:	80 °C
Sample Line Temp.:	110 °C
Transfer Line Temp.:	120 °C
Vial Stirring:	Off
Vial Volume:	20 mL
Vial Heat-Retention Time:	45 min
Vial Pressurization Time:	1 min
Vial Pressure:	75.0 kPa(N_2)
Loading Time:	0.5 min
Needle Flush Time:	5 min
Injection Volume:	1 mL
Load Equilib. Time:	0 min

*1 P/N: 227-36077-01

■ Analysis of Class 1 Standard Solution (Water-Soluble Sample)

The analysis results for Procedure A using a H_2 carrier are shown in Fig. 1. The S/N ratio and repeatability values for each peak are shown in Table 2. Table 3 shows the S/N ratio and repeatability values for each peak when using a He carrier as a reference.

Using a H_2 carrier, the results obtained with Procedure A satisfied the requirements of the USP, which specifies that "the S/N ratio for 1,1,1-trichloroethane in the Class 1 standard solution is not less than 5. "

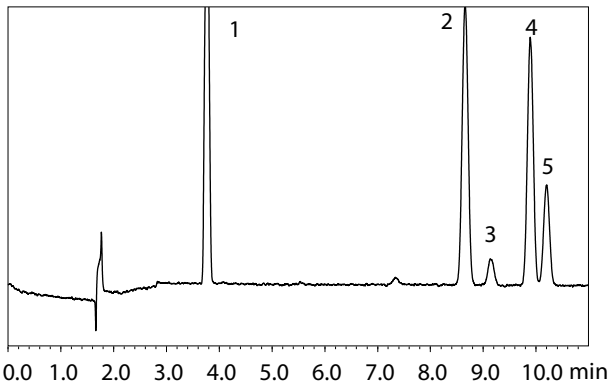

Fig. 1 Chromatogram of Class 1 Standard Solution by Procedure A (Water-Soluble Sample)

Table 2 S/N Ratio and Repeatability of Class 1 Standard Solution (Procedure A) Using H_2 Carrier

Peak No.	Compound	S/N Ratio *1 (n=4)	%RSD *1 (n=4)
1	1,1-Dichloroethane	93	1.99
2	1,1,1-Trichloroethane	123	1.45
3	Carbon tetrachloride	15	3.94
4	Benzene	145	2.48
5	1,2-Dichloroethane	57	2.60

*1 The S/N ratio and relative standard deviation (%RSD) values are reference values and not intended to be guaranteed values.

Table 3 S/N Ratio and Repeatability of Class 1 Standard Solution (Procedure A) Using He Carrier

Peak No.	Compound	S/N Ratio *1 (n=4)	%RSD *1 (n=4)
1	1,1-Dichloroethane	131	1.44
2	1,1,1-Trichloroethane	150	1.64
3	Carbon tetrachloride	13	7.30
4	Benzene	188	0.66
5	1,2-Dichloroethane	76	0.81

*1 The S/N ratio and relative standard deviation (%RSD) values are reference values and not intended to be guaranteed values.

■ Analysis of Class 2 Standard Solution (Water-Soluble Sample)

Fig. 2 shows the analysis results for a Class 2A and Fig. 3 for a Class 2B standard solution. Methyl isobutyl ketone (MiBK), a component newly added to USP General Chapter <467> Residual Solvents for Class 2A was also measured. (Results with the H_2 carrier are indicated in black, the He carrier in pink, and for MiBK with the H_2 carrier in blue.) Satisfactory system suitability results were also obtained, for which the USP specifies that "the resolution between acetonitrile and methylene chloride in the Class 2A standard solution is not less than 1.0" when using Procedure A.

* The resolution values shown in Fig. 2 are intended as reference values and are not guaranteed.

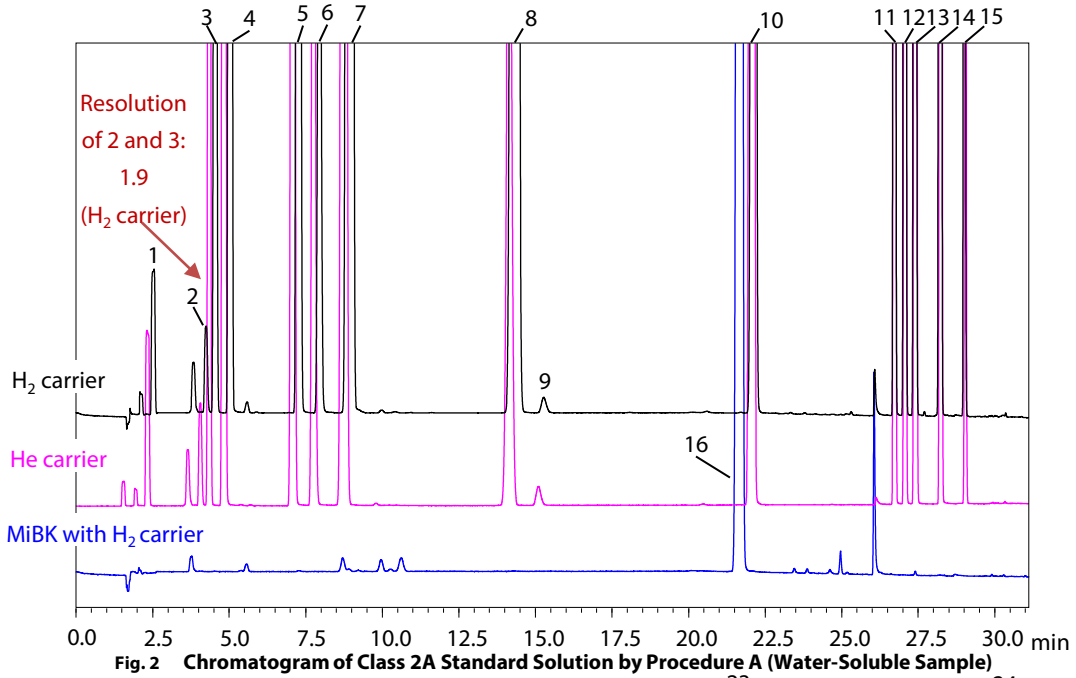

Fig. 2 Chromatogram of Class 2A Standard Solution by Procedure A (Water-Soluble Sample)

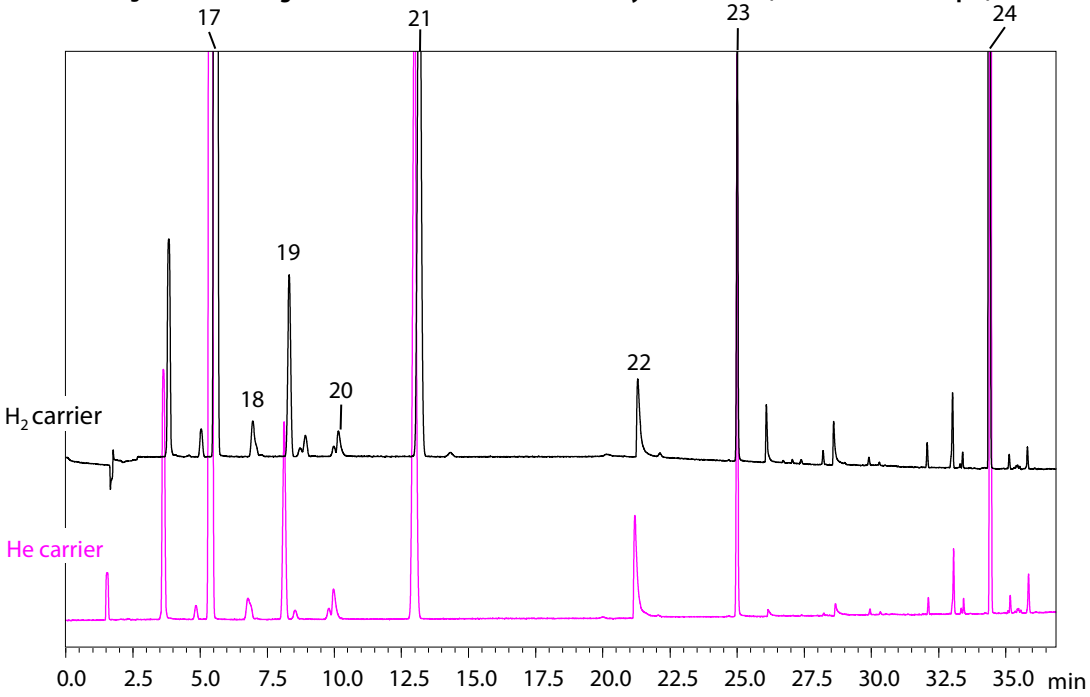

Fig. 3 Chromatogram of Class 2B Standard Solution by Procedure A (Water-Soluble Sample)

■ Conclusion

Using a H_2 carrier gas, the analysis achieved the accuracy levels required by USP Chapters <467> and <1467>. The Nexis GC-2030 features a hydrogen sensor to ensure safe H_2 usage. Hydrogen sensors detect potential leaks early. When hydrogen leakage increases, the main power supply is switched off to prevent accidents. Using a H_2 carrier can help reduce lab costs. For information about using a N_2 carrier for analysis of residual solvents in pharmaceuticals using water-soluble samples, refer to Application News No. G325.

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