SHIMADZU APPLICATION NEWS

LA180-E005

● GAS CHROMATOGRAPHY

No.G209

Analysis of Residual Solvents in Pharmaceuticals (Part 5) Comparison of Headspace GC Sensitivity when Using Different Dilution Solvents

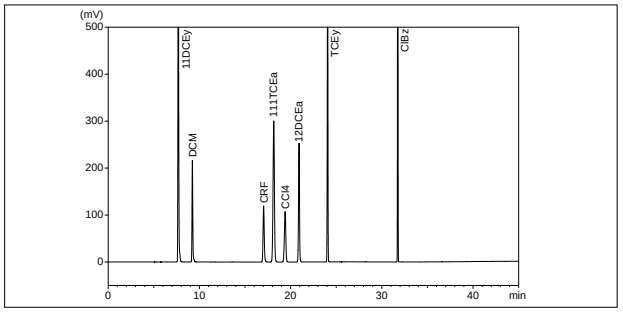
The Shimadzu Application News (GC) “Analysis of Residual Solvents in Pharmaceuticals” series has previously introduced the following items.
G185 (Part 1) Separation conditions and elution order of solvents specified as classes 1 and 2 in the guidelines
G186 (Part 2) Introduction of methods IV and V in USP 23 (using HSS series)
G193 (Part 3) Introduction of headspace GC for solvents specified as classes 1 and 2 in the guidelines
G204 (Part 4) Introduction of method IV in USP 24 (using TurboMatrix HS series)
Residual solvents in pharmaceuticals can be analyzed by dissolving pharmaceuticals in an appropriate solvent and injecting the solution directly into the GC. However, in the future, headspace GC, where the solution is sealed in a vial, kept warm to evaporate highly volatile components into the gas phase for analysis, will be the mainstream.
In headspace GC, the sensitivity for the target components greatly differs depending on the degree of evaporation of the target components when the sample solvent is heated in the vial.
This analysis example focuses on the difference of sensitivity for target components when using different solvents (diluent for standard solvent) to dissolve the pharmaceuticals.
The target components are substances designated in the guidelines as classes 1 and 2 (and THF).
Used solvents were water (specified in USP and EP), DMSO (specified in some of the USP pharmaceutical ordinances) and DMF (specified in EP 2001 for water-insoluble substances).
For all components, standard solutions of 100ppm concentration were sealed in vials and kept warm for analysis. The heating conditions were 60min at 80˚C for DMSO and water (USP conditions and EP water conditions) and 45min at 105˚C for DMF (DMF conditions in EP).
Table 1 shows the relative sensitivity of each component when the peak area with water used as diluent is taken as 1. (“>1” indicates sensitivity higher than when using water, and “1/100>” indicates 1/100 or less.)
Most components show higher solubility in DMSO and DMF than in water, which means they are more difficult to evaporate. Therefore, sensitivity for these components remarkably decreases when using DMSO or DMF, in stead of water, for solvent.

Table 1 Relative sensitivities of components in DMF and DMSO compared to those in water

	DMSO				DMF			
Class 1	>1	>1/10	>1/100	1/100>	>1	>1/10	>1/100	1/100>
Benzene (Bz)			○				○	
Tetrachloroethane (CCl4)			○				○	
1,2-Dichloroethane (12DCEa)			○				○	
1,1-Dichloroethylene (11DCEy)			○				○	
1,1,1-Trichloroethane (111TCEa)			○				○	
Class 2								
Acetonitrile (AcNt)		○				○		
Chlorobenzene (ClBz)				○				○
Chloroform (CRF)				○			○	
Cyclohexane (cycC6)			○				○	
Dichloromethane (DCM)			○				○	
1,2-Dimethoxyethane (12DMOEa)		○			○			
N,N-Dimethylformamide (DMF)								
N,N-Dimethylacetamide (DMAc)								
1,4-Dioxane (14-D)		○			○			
2-Ethoxyethanol (Etcel)								
Ethylene glycol (EG)								
Formamide (FAm)								
Hexane (C6)		○				○		
Methanol (MeOH)		○			○			
2-Methoxyethanol (Mecel)								
Methylbutylketone (MBK)			○				○	
Methylcyclohexane (MecycC6)			○				○	
N-methylpyrrolidone (N-Meprldn)								
Nitromethane (NtMe)			○			○		
Pyridine (Pry)		○				○		
Sulfolane (Sulfln)								
Tetralin (Tetrln)								
Toluene (Tol)			○				○	
1,1,2-Trichloroethylene (TCEy)			○				○	
Xylene (EB,p-X,m-X,p-X)				○				○
THF		○				○		

■ Headspace gas chromatograms of 100ppm organic solvents standard in water

Chromatogram of Chlorinated Solvents



Chromatogram of Non-Chlorinated Solvents

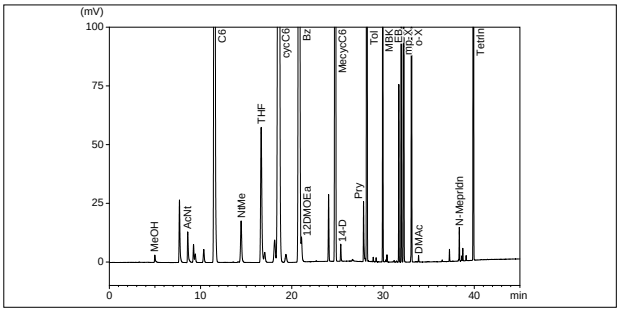
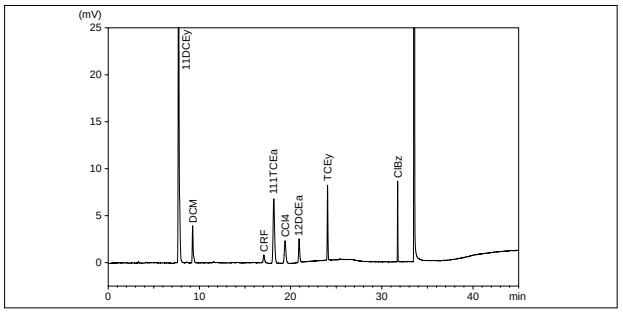


Fig.1 Headspace Gas Chromatograms of Solvents in Water

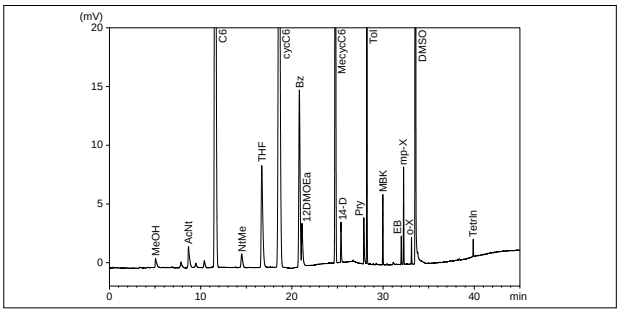
■ Headspace gas chromatograms of 100ppm organic solvents standard in DMSO

Chromatogram of Chlorinated Solvents



*The ordinate is enlarged by 20 times that of Fig. 1.

Chromatogram of Non-Chlorinated Solvents

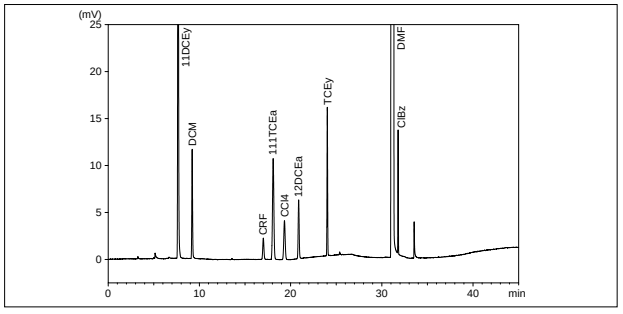


*The ordinate is enlarged by 5 times that of Fig. 1.

Fig.2 Headspace Gas Chromatograms of Solvents in DMSO

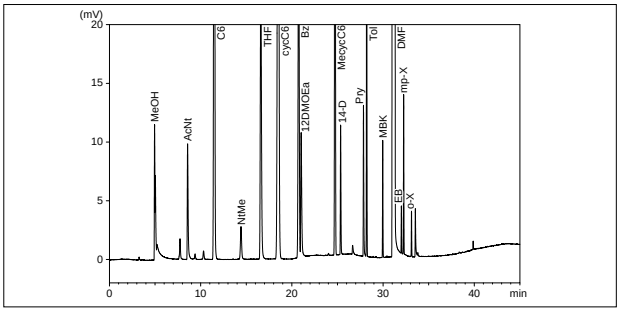
■ Headspace gas chromatograms of 100ppm organic solvents standard in DMF

Chromatogram of Chlorinated Solvents



*The ordinate is enlarged by 20 times that of Fig. 1.

Chromatogram of Non-Chlorinated Solvents



*The ordinate is enlarged by 5 times that of Fig. 1.

Fig.3 Headspace Gas Chromatograms of Solvents in DMSO

Table 2 Analytical conditions

Model	: TurboMatrix HS-40+GC-2010	Carrier Gas	: He, 35cm/sec, Split Ratio:1:5
Column	: DB-624 30m×0.32mmi.d. film:1.8μm	Sample Thermostatting	: 80˚C 60min (in Water, in DMSO)
Column Temp.	: 40˚C (20min)-240˚C at 10˚C/min		110˚C 45min (in DMF)
Inj. Temp.	: 140˚C, Det Temp.:260˚C	Headspace Injection Volume	: 1mL

SHIMADZU

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