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Using GCMS to Test for Residual Solvents in Pharmaceuticals

1 Introduction

The HS-GC-FID method is used to test for residual solvents in pharmaceuticals, but GC-MS is useful for identifying peaks in close proximity or for qualifying unknown peaks. However, to qualify peaks detected by GC-FID using GC-MS requires matching chromatogram patterns. The advanced flow controller (AFC) in GC-2010 Plus systems includes constant linear velocity control as standard functionality. This allows achieving similar retention time and separation patterns in GC-FID and GC-MS chromatograms by specifying the same linear velocity setting, provided the columns are identical or columns with the same phase ratio are used.

2 Analytical Conditions to Test for Residual Solvents in Pharmaceuticals

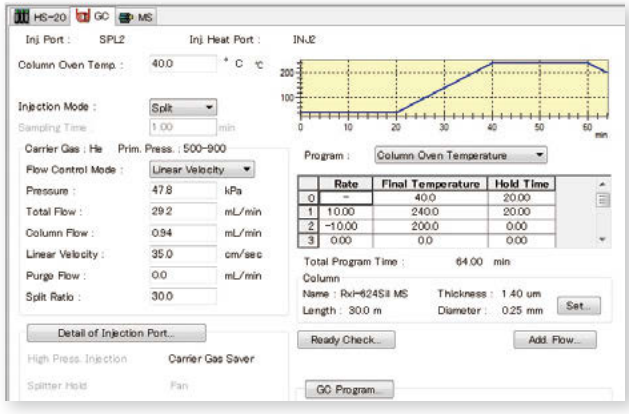
Testing for residual solvents in pharmaceuticals involves using a separation column with a 0.53 mm (or 0.32 mm) internal diameter, 30 m length, and 3.0 µm (or 1.8 µm) thick cyanopropyl phenyl-based liquid phase and separation conditions with a linear carrier gas speed of 35 cm/sec (Procedure A). However, those separation conditions cannot be achieved using GC-MS, due to the negative pressure (vacuum) at the column outlet. Therefore, the typical method used to obtain similar chromatogram patterns is to downsize the column to one with a small internal diameter, so that the phase ratio (ratio of column internal diameter to film thickness) is the same.

SH Rxi-624sil MS
0.32 mm I.D., 30 m long, and 1.8 µm film thickness

SH Rxi-624sil MS
0.25 mm I.D., 30 m long, and 1.4 µm film thickness

This results in similar chromatogram patterns using the same linear velocity of 35 cm/sec.

Control by the AFC takes into consideration the difference in column outlet pressure between GC and GC-MS. For HS-GCMS analysis, it simply requires changing the column and specifying a 35 cm/sec linear velocity in the method parameter selection window in GCMSsolution. During analysis, the AFC controls the carrier gas automatically, which eliminates the inconvenience of having to adjust pressure or other settings.

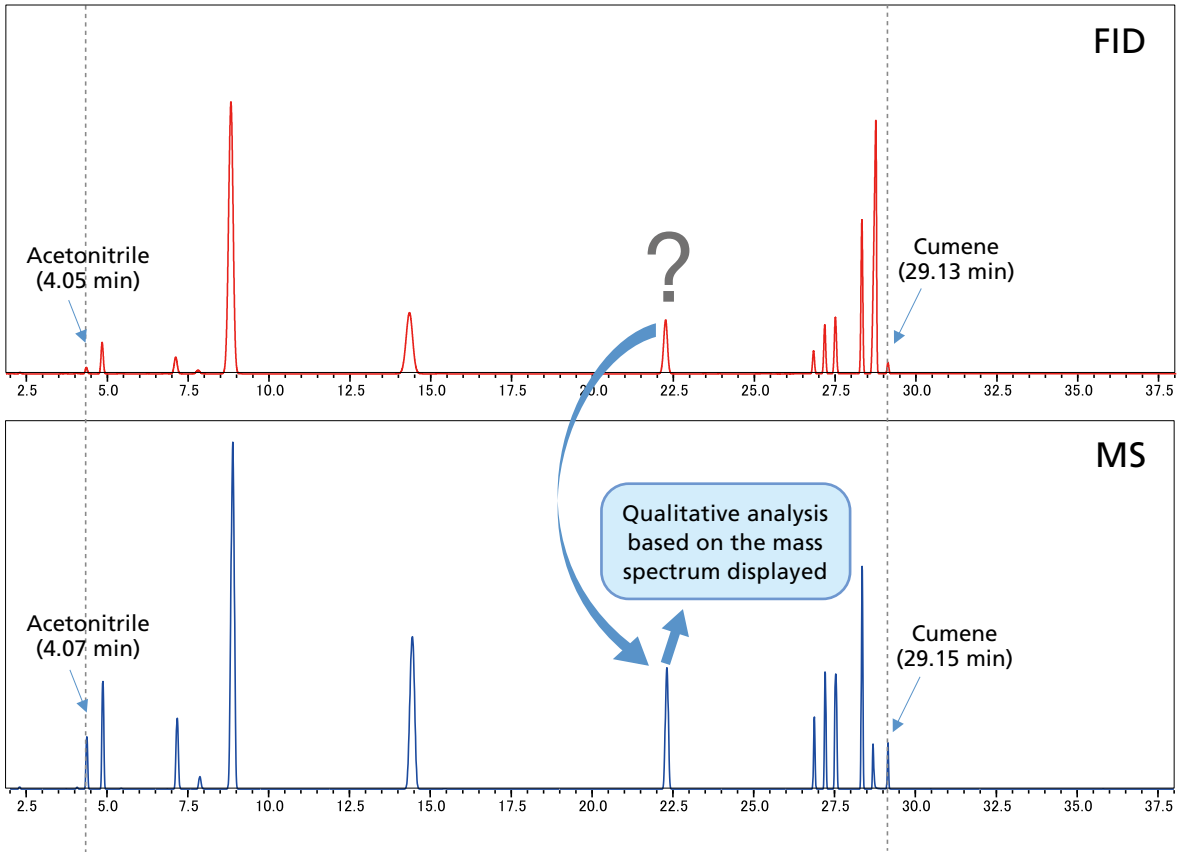


GCMS-QP2020 + HS-20 + FID-2010 Plus Detector

By including an FID detector in the HS-GCMS system, either analytical method can be used. Contact a Shimadzu representative regarding changing the system configuration, which can be modified to accommodate various user requirements.

3 Comparison of GC-FID and GC-MS Chromatograms

After using a GC-FID system to acquire data from a Class 2 standard solution A, data were acquired using a GC-MS system with the same linear velocity condition (35 cm/sec). Then the resulting chromatograms were compared. The comparison shows that the shift in retention times between FID and MS data was 0.02 minutes (1.2 seconds) for acetonitrile, which elutes early, and for cumene, which elutes late. In addition, both chromatograms were similar, with approximately the same separation patterns.



The GC-MS data showed a peak at roughly the same retention time as for the unknown peak detected by the GC-FID system. This peak can be identified easily by qualitative analysis, such as by displaying the mass spectrum and using an MS spectral library to search for a similar peak pattern.

4 Summary

If a HS-GC-MS system is used for qualitative analysis in testing for residual solvents in pharmaceuticals, it is important that the chromatogram pattern obtained is similar to the chromatogram obtained from HS-GC-FID analysis. The constant linear velocity control mode for the AFC unit included in Shimadzu GC-MS systems can be used in combination with a Shimadzu HS-20 headspace sampler. Even if the different-sized columns are used for HS-GC-FID and HS-GC-MS analysis, chromatograms with similar retention times and separation patterns can be obtained easily by using columns with the same phase ratio and by specifying the same linear velocity setting, which means GC-MS data can easily be used for qualitative analysis.

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Printed in Japan 3655-02707-20AIT