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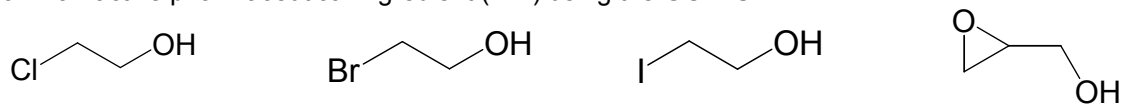
Application Data Sheet

No.41

GC-MS
Gas Chromatograph Mass Spectrometer

Analysis of Potential Genotoxic Impurities in Active Pharmaceutical Ingredients (3)
-Analysis of Haloalcohols and Glycidol Part 1-

Haloalcohols (Fig. 1) are used as synthetic materials in pharmaceuticals, and are considered potential genotoxic impurities (PGI). In addition, glycidol (Fig. 1) has been identified as a cancer-causing agent, and has been assigned to Group 2A (probably carcinogenic to humans) in terms of carcinogenic risk by the International Agency for Research on Cancer (IARC). This Application Data Sheet introduces analysis of haloalcohols and glycidol in an active pharmaceutical ingredient (API) using the GC-MS.



2-Chloroethanol　2-Bromoethanol　2-Iodoethanol　Glycidol

Fig. 1 Compound Structures of Typical Haloalcohols and Glycidol

Experimental

Many APIs are compounds with a high boiling point, and can cause GC-MS and column contamination; therefore, it is critical to extract the target compounds from the API matrix prior to analysis by GC-MS. Haloalcohols and glycidol are highly polar, making them difficult to extract with organic solvents. Accordingly, the target compounds were subjected to trimethylsilyl (TMS) derivatization before a solvent extraction was performed utilizing water and dichloromethane, thereby removing as much of the API as possible [1]. In addition, 1,1,2,2-bromoethanol-D4 was utilized as the internal standard substance, and 50 ng of that was added to 200 µL of solution. Fig. 2 shows the detailed pretreatment procedure.

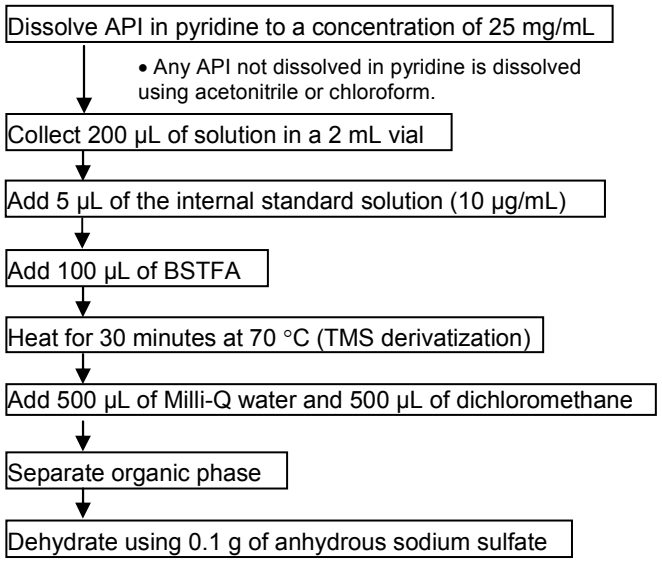


Fig. 2 Sample Preparation Procedure

Analytical Conditions

FASST (Fast Automated Scan/SIM Type), which is capable of simultaneous Scan and SIM measurements, was used as the measurement mode. The analysis conditions are shown in Table 1.

Table 1 Analytical Conditions

GC-MS	: GCMS-QP2010 Ultra
Column	: Rtx-200 (Length 30 m × 0.25 mm I.D., df = 0.25 µm)
Glass Liner	: Deactivated Split insert with glass wool (P/N: 225-20803-01)
[GC]	
Injection Temp.	:280 °C
Column Oven Temp.	:50 °C (5 min) → (10 °C/min) → 100 °C → (20 °C/min) → 320 °C (3 min)
Injection Mode	:Split
Flow Control Mode	:Linear velocity (32.4 cm/sec)
Split Ratio	:30
Injection Volume	:1.0 µL
[MS]	
Interface Temp.	:280 °C
Ion Source Temp.	:230 °C
Measurement Mode	:FASST (simultaneous Scan/SIM measurements)
Scan Mass Range	:*m/z* 30–450
Scan Event Time	:0.2 sec
SIM Event Time	:0.3 sec
SIM Monitoring *m/z*	:
2-chloroethanol-TMS	93, 95
2-bromoethanol-TMS	181, 183
2-bromoethanol-D4-TMS	187
Glycidol-TMS	101, 59
2-iodoethanol-TMS	185, 229

Results

Fig. 3 shows the total ion current chromatogram of a 25 µg/mL standard sample (equivalent to 1000 ng/mg in the pharmaceuticals), and Fig. 4 shows the scan mass spectra.

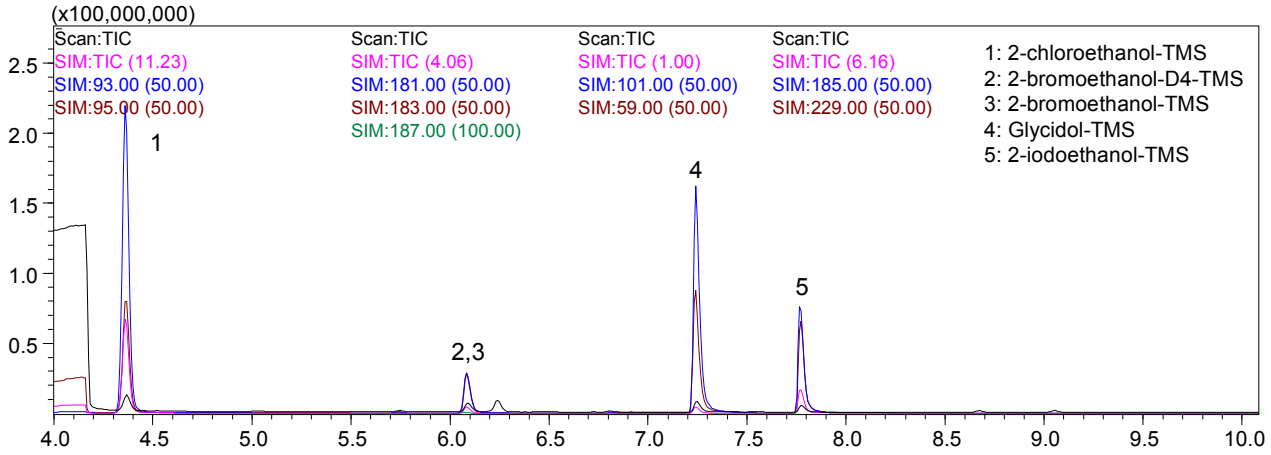


Fig. 3 Total Ion Current Chromatogram

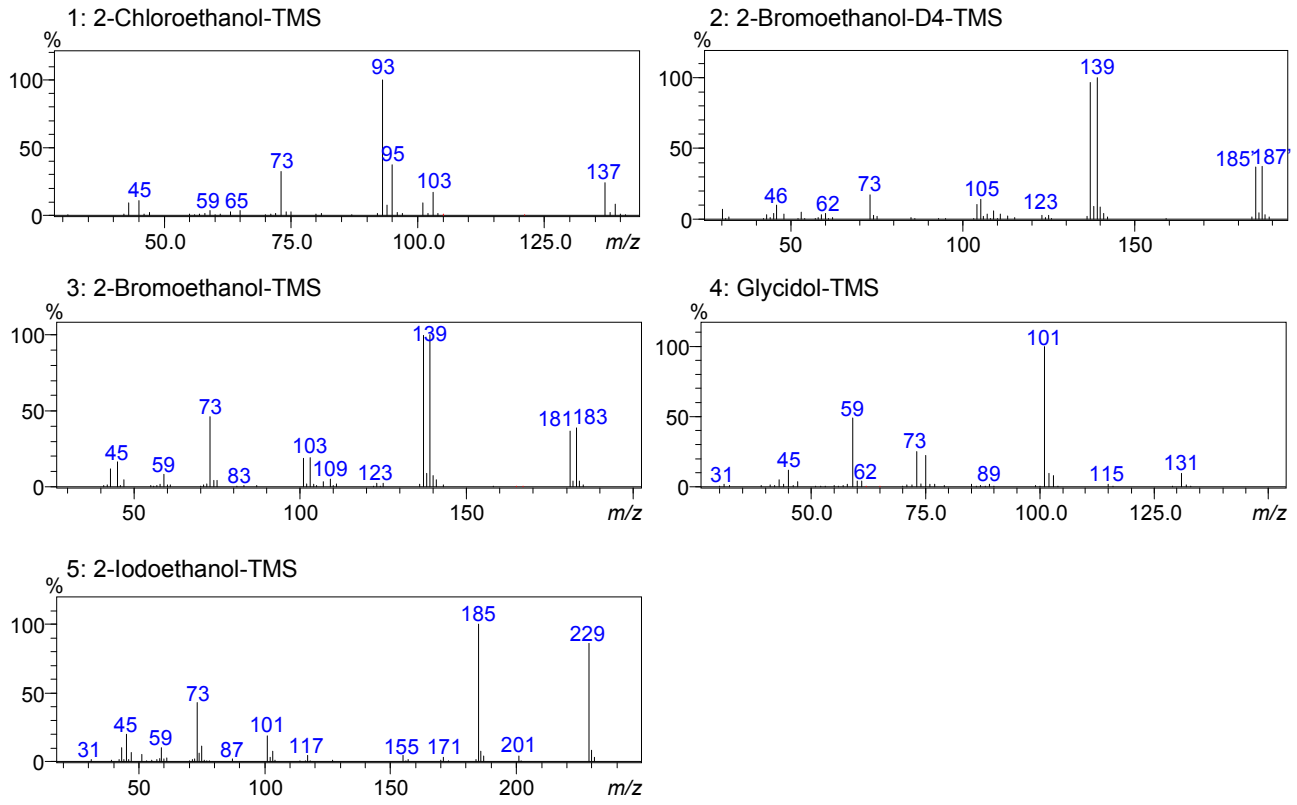


Fig. 4 Scan Mass Spectra of Haloalcohols and Glycidol

Reference

[1] Frank David, Karine Jacq, Pat Sandra, Andrew Baker and Matthew S. Klee: Analysis of potential genotoxic impurities in pharmaceuticals by two-dimensional gas chromatography with Deans switching and independent column temperature control using a low-thermal-mass oven module, Anal Bioanal Chem, 396, 1291-1300 (2010)

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