

Application News

No. GC-19-ADI-037

Nexis GC-2030 with HS-20

Next Industry Standard Nexis GC-2030 with HS-20 made drug substance residual solvent analysis simpler with constant flow mode

□ Introduction:

Method transfer is no more challenge to Shimadzu new Nexis GC-2030 with HS-20 sampler for residual solvent analysis in drug substance as Nexis GC-2030 can now run in constant flow as an additional carrier gas flow mode. This enables smooth method transfer between different makes of GC. Furthermore, GC-2030 can use the constant linear velocity and constant pressure modes with multistage programming. All control modes can be used with advanced flow technologies, such as backflush, detector switching which leads to better gains in productivity.

In this application, data obtained from Make A for the residual solvents analysis of drug substance Sitagletin was compared with the data generated on Nexis GC-2030 coupled with HS-20 to ascertain repeatability and no carry over during method transfer.

□ Experimental:

Multiple residual solvent standard was selected to establish ease of method transfer on Nexis GC-2030 coupled with HS-20. Retention time, area %RSD and carryover test were compared.

Sample preparation:

Weighed and dissolved 0.3 g methanol, 0.5 g ethanol, 0.5 g isopropyl alcohol, 0.041 g acetonitrile, 0.06 g dichloromethane, 0.5 g tert-butyl methyl ether, 0.5 g ethyl acetate and 0.625 g triethylamine in dimethylacetamide (DMAC) in a 100 mL volumetric flask (DIL-1).

Diluent blank preparation : 0.1 g piperazine + 1.0 mL DMAC in 20 mL headspace vial.

STD Preparation for RSD check : 0.1 g piperazine + 1.0 mL Std. (DIL-1) in 20 mL headspace vial.

The final batch was submitted as:

1. 2 Diluent blank vials
2. 6 Vials for RSD check
3. 2 Diluent blank vials for carry over check

□ Analytical Conditions:

Headspace parameters:

Mode	Loop
Oven Temp.	75 °C
Sample Line Temp.	85 °C
Transfer Line Temp.	95 °C
Shaking Level	5
Equilibrating Time	20.0 min
Pressurize Gas Pressure	103 kPa
Load Time	0.5 min
Injection Time	1.0 min
GC Cycle Time	35.33 min

Chromatographic parameters:

Column	SH-Rtx-624 (30 m x 0.32 mm x 1.8 µm)		
Column Flow	0.5 mL/min	Flow Mode: Constant Flow	
Split Ratio	10.0		
Carrier gas	Helium		
Column oven program	Rate °C /min	Temperature °C	Hold Time (min)
		40.0	10.0
	15.0	180.0	6.0
FID temperature	270 °C		
APC Pressure programming	Rate kPa/min	Pressure(kPa)	Hold Time (min)
		103.0	2.0
	50.00	350.0	18.39

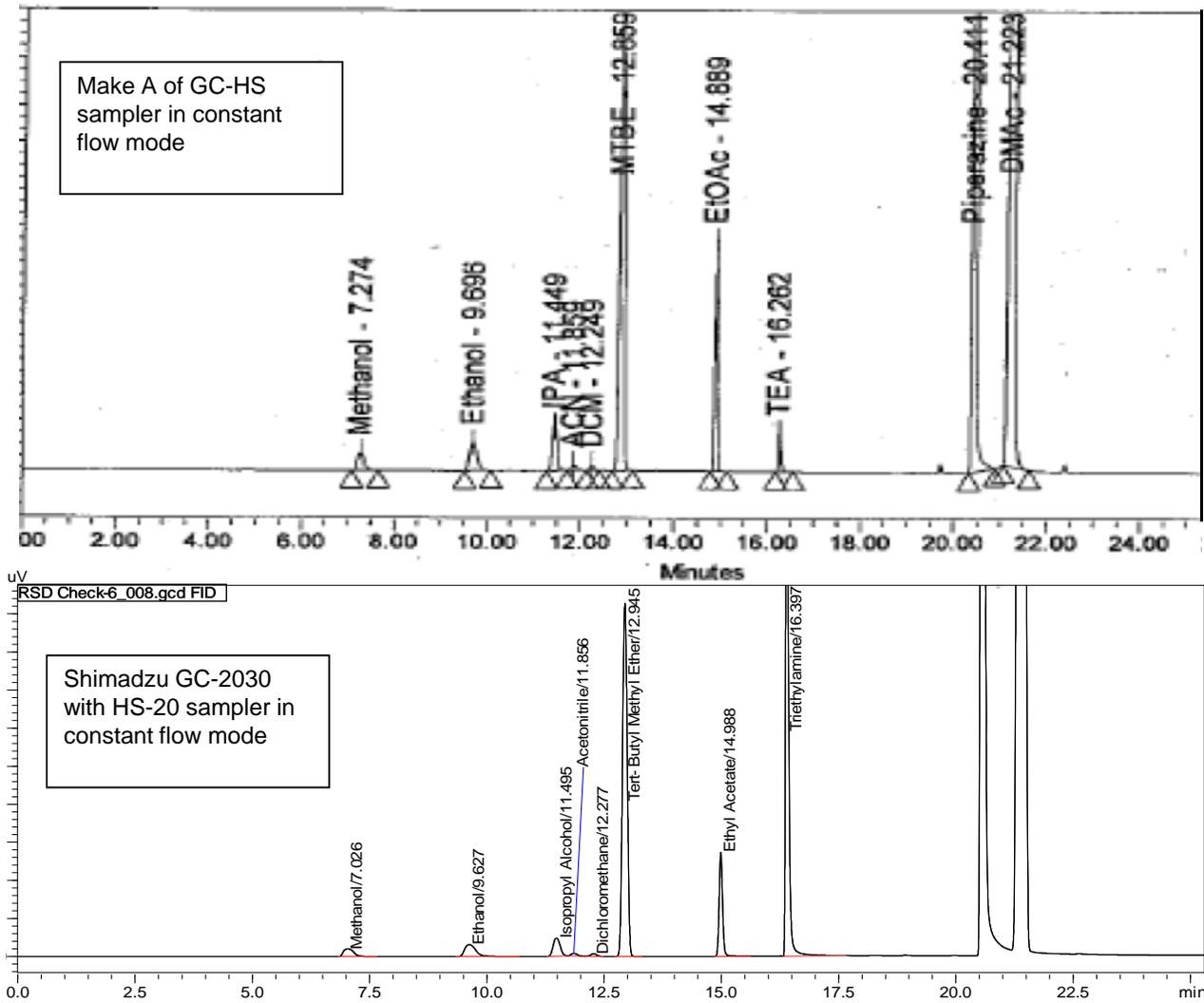


Figure 1: Comparative chromatographic peak profile on Make A of GC-HS and Shimadzu Nexis GC-HS

Table 1: Comparison summary of Retention times (RT)

Sr.No.	Solvent	RT in min. Make A GC-HS	RT in min. Shimadzu GC-HS	RT Difference in min.
1	Methanol	7.274	7.029	0.245
2	Ethanol	9.696	9.625	0.071
3	Isopropyl Alcohol	11.449	11.488	0.039
4	Acetonitrile	11.859	11.852	0.007
5	Dichloromethane	12.249	12.275	0.026
6	Tert-Butyl Methyl Ether	12.859	12.942	0.083
7	Ethyl Acetate	14.889	14.987	0.098
8	Triethylamine	16.262	16.399	0.137

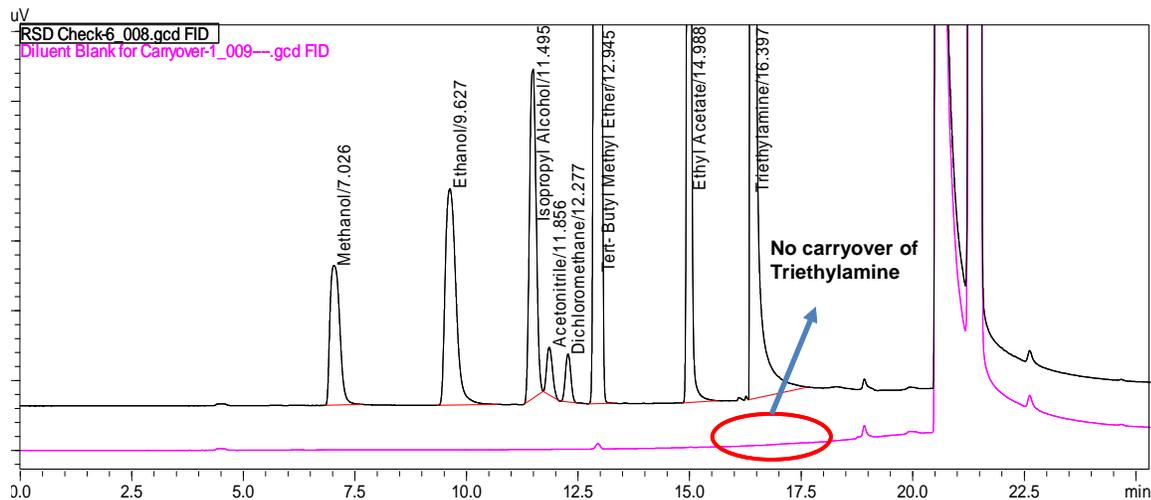


Figure 2: Overlay of Standard solvent mixture and diluent blank on Nexis GC-2030 with HS-20

□ Results and Discussion:

The method transfer was very much easy with new advance flow and pressure controller (AFC & APC) that have been developed in Nexis GC-2030 which includes a own CPU. It supports carrier gas constant linear velocity control, constant flowrate control, constant pressure control, and various other control modes which achieves exceptionally high reproducibility for ultra-high-speed and ultra-high-precision control modes. Comparative chromatographic peak profile and summary of retention times are shown in Figure 1 and Table 1 respectively. Figure 2 depicts no carry over for any solvents and Table 2 shows area %RSD and carry over for mixture of residual solvent standard.

Table 2 Area %RSD and carryover summary

Sr.No.	Solvent	Conc. in ppm	Area %RSD (n=6)	Carryover
1	Methanol	300	2.15	Nil
2	Ethanol	500	2.11	Nil
3	Isopropyl Alcohol	500	2.06	Nil
4	Acetonitrile	41	2.14	Nil
5	Dichloromethane	60	4.32	Nil
6	Tert-Butyl Methyl Ether	500	1.73	Nil
7	Ethyl Acetate	500	1.79	Nil
8	Triethylamine	625	1.65	Nil

□ Conclusion:

1. With the new advance flow and pressure controller (AFC & APC) in Nexis GC-2030, it is very easy to adopt any flow control modes to achieve trace level results that are highly reproducible.
2. Very short transfer line in headspace sampler ensures least or no carry over which is the characteristics feature of Shimadzu's HS-20 headspace system.
3. Constant flow mode made method transfer very easy for residual solvent analysis without any compromise on reproducibility and sensitivity.

