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Application News

GC-MS HS-20 NX Trap/GCMS-QP 2020 NX

Analysis of Thermal Extracts from an Eye Drop Container via the Trapped Headspace (THS) Method

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User Benefits

- With more than 20 times the sensitivity of static headspace (SHS) analysis, this system can detect extracts from pharmaceutical packaging with high sensitivity.
- With an electronic cooling trap, the system can analyze everything from low to high boiling point compounds in a single analysis cycle.
- The system can also switch between trap mode and loop mode, depending on the concentration.

■ Introduction

Compounds eluted from pharmaceutical packaging are transferred to the pharmaceuticals, and the ensuing risk to humans from continuous exposure is a focus of interest. These substances are referred to as extractables and leachables, which together are abbreviated as E&L.

Methods for measuring them are being sought at present, and various suggestions have been proposed. When screening for volatile and semi-volatile compounds, high sensitivity results are comparatively easy to obtain with the combination of GCMS and the trapped headspace (THS) method, which is why it is a focus of interest.

The HS-20 NX Trap is a trap headspace sampler equipped with an electronic cooling trap. It is optimal for thermal extraction as it can be heated up to 300 °C.

In trap mode, which uses the trapped headspace (THS) method, basically the entire volume of the headspace is concentrated into the trap. As a result, in comparison with loop mode, which uses the static headspace (SHS) method, more than 20 times the sensitivity is obtained with THS, which approaches the sensitivity of thermal desorption (TD).

This articles introduces a comparison of the measurement results for thermal extracts from an eye drop container using SHS, THS, and TD.

■ Instrument Configuration and Analysis Conditions

The analysis conditions for the thermal extracts obtained using the GCMS-QP2020 NX and the HS-20 NX Trap are shown in Table 1.

Table 1 Analysis Conditions

GCMS Analysis Conditions	
Model:	GCMS-QP2020 NX
Column:	SH-I-5Sil MS (P/N: 221-75954-30) (0.25 mm I.D. × 30 m, d.f.= 0.25 µm)
Column Temp.:	50 °C (2 min) – 10 °C/min – 320 °C (6 min) Total 35 min
Injection Mode:	Split 1 : 20
Carrier Gas Controller:	Constant Linear Velocity Mode (He)
Linear Velocity:	44.4 cm/sec
Transfer Line Temp.:	250 °C
Ion Source Temp.:	200 °C
SCAN:	*m/z* 20-600
HS Analysis Conditions	
Oven Temperature:	150 °C
Equilibration Time:	15 min
Sample Line Temp.:	250 °C
Transfer Line Temp.:	250 °C
Vial Stirring:	Off
Vial Volume:	20 mL
Vial Pressurization Time:	1.0 min
Vial Press. Equilib. Time:	0.1 min
Loading Time:	0.5 min
Load Equilib. Time:	0 min
Multi Injection:	3
Vial Pressure:	100.0 kPa (He)
Trap Cooling Temp.:	-10 °C
Trap Heating Temp.:	250 °C
Trap Adsorbent:	Tenax TA 60/80 mesh 37 mg
Injection Time:	5.0 min
Needle Flush Time:	15.0 min

■ Extractables and Leachables

Extractables are defined as compounds extracted from pharmaceutical packaging using solvents or by heating. In contrast, leachables are compounds that are transferred to the pharmaceutical agent from the pharmaceutical packaging under routine storage conditions. Theoretically, leachables are produced from extractables. However, in actuality leachables are not limited to extractables. The compounds targeted for thermal extraction in this experiment are shown in Table 2.

Table 2 Compounds Targeted for Thermal Extraction

Compound	Possible source
Nonanal	Break down of lubricant or stabilizer
Naphthalene	Break down of fire retardant
2,6-Bis(tert-butyl)-4-ethylphenol	Break down of antioxidant
DEP	Plasticizer
DiBP	Plasticizer
DBP	Plasticizer

■ Comparison of Analysis Method

With THS, the volume of gas phase concentrate is approximately 1/30 that of TD. However, the sample volume that can be filled is more than 100 times larger, so the difference in sensitivity becomes a factor of 10 (Table 3). In practice, the results indicate that the target compounds are sufficiently detected and qualified using GCMS. In addition, wide-mouth vials reduce the risk of contamination because they can be filled even if the sample has not been finely ground. (Fig. 1)

Table 3 Comparison of Analysis Methods

	THS	TD
Sample Volume	Approx. 1300 mg	Approx. 20 mg
Amount of Concentrate	Approx. 20 mL	Approx. 600 mL
Filling with the Sample	Easy	Difficult
Heating Temperature	Up to 300 °C	Up to 400 °C

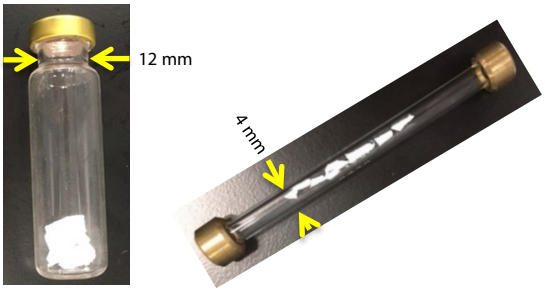

Fig. 1 Filling with the Sample (Left: Headspace Vial; Right: TD Tube)

■ Example of the Measurement of Thermal Extracts from an Eye Drop Container

From Fig. 2, it is evident that with the LDPE nozzle and bottle, the intensity of pyrolytic compounds is smaller than with the HDPE cap. However, nonanal and other target compounds were detected with sufficient sensitivity. The measurement results for the nozzle via SHS and THS are shown in Fig. 3.

Nonanal, which was basically not detected with SHS, was clearly identified with THS, at an intensity sufficient to be identified in a library search. In comparison with TD in Fig. 4, it is evident that an intensity of 1/10 or higher was obtained with THS.

Compound	Cap	Bottle	Nozzle
Nonanal		✓	✓
Naphthalene	✓	✓	✓
2,6-Bis(tert-butyl)-4-ethylphenol		✓	
DEP	✓	✓	✓
DiBP	✓	✓	✓
DBP	✓	✓	✓

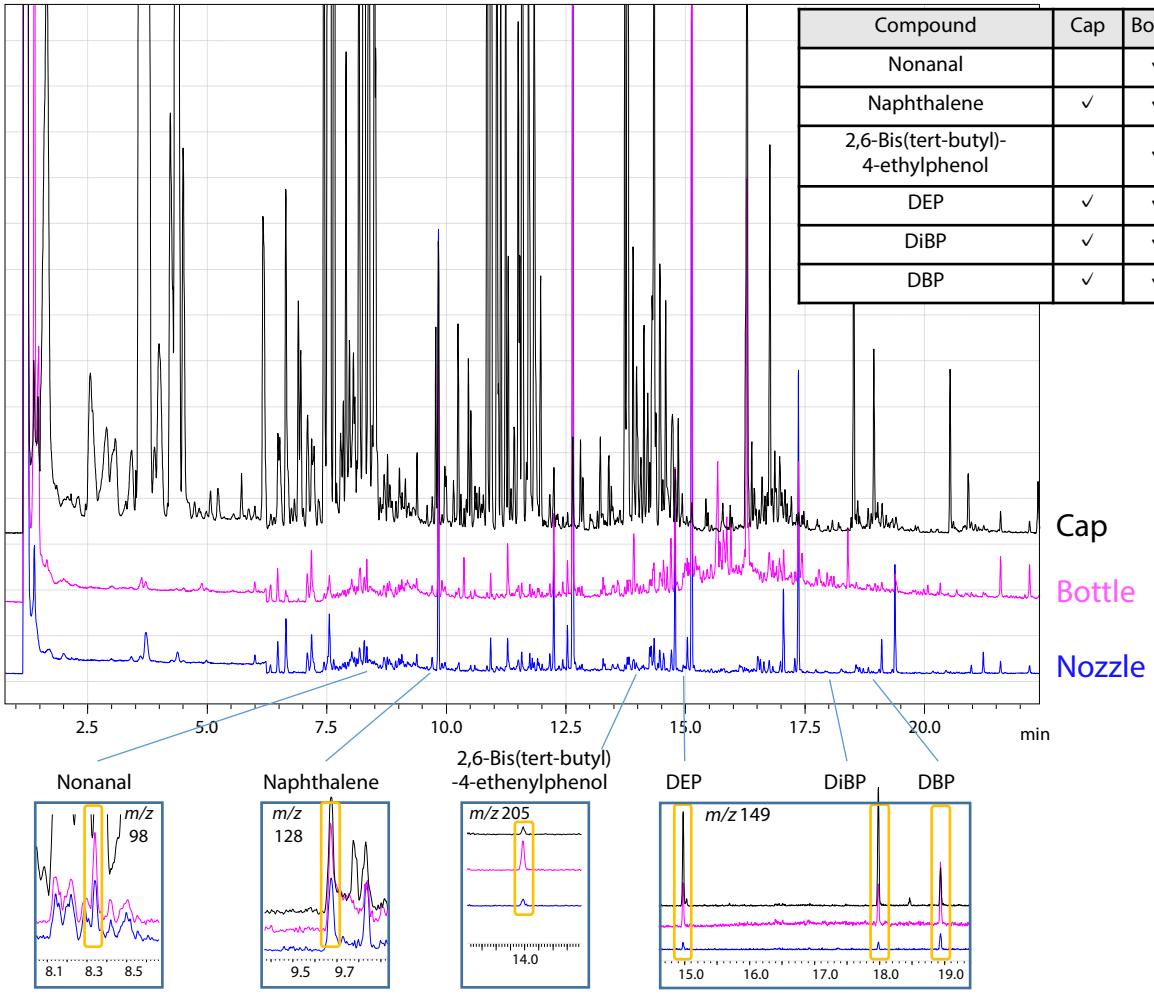

Fig. 2 Thermally Extracted Compounds from an Eye Drop Container

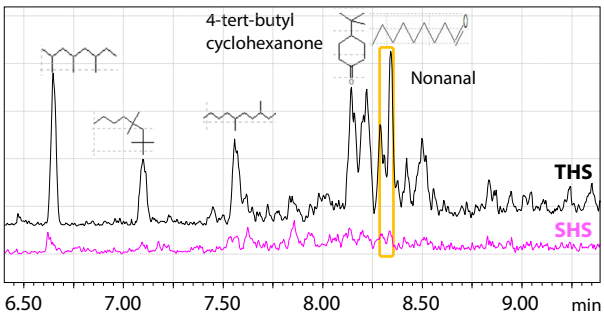

Fig. 3 Nozzle Measurement Results via SHS and THS

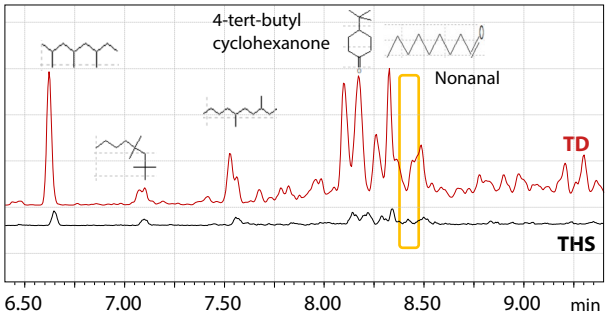

Fig. 4 Nozzle Measurement Results via THS and TD

■ Conclusion

THS can be used for measurement of thermal extracts from pharmaceutical packaging, the same as TD. In comparison with TD and other concentration systems, high sensitivity measurements can be performed inexpensively and with quick extraction. Since the system can switch between trap mode and loop mode, rather than being a dedicated E&L system, it can be utilized for a wide range of applications including the analysis of residual solvents, impurities, and diffused gases.

01-00219-EN First Edition: Sep. 2021

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