

## GERSTEL AppNote 277

# Determination of Butylated Hydroxytoluene in Plastic and Saline Solution: An Extractable and Leachable Study

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## Keywords

Extractables and leachables, direct thermal extraction (DTE), stir bar sorptive extraction (SBSE), gas chromatography, and mass spectrometry.

## Abstract

Extractable and leachable (E&L) studies are routinely conducted for products such as medical devices, pharmaceuticals, and packaging for these types of products. The aim of these studies is to make sure that nothing is emitted from the product that can be harmful to the consumer. Harmful compounds can be from the product itself, residuals from manufacturing or from the packaging used for the product.

This document discusses a study using direct thermal extraction to determine leachables from a plastic bottle containing a saline enema solution. Stir Bar Sorptive Extraction (SBSE) was used to quantify the compound of interest in the saline solution.

## Introduction

Direct thermal extraction (DTE) is a technique in which a solid or liquid sample (in a suitable holder) is heated with inert gas flow, and the evolved analytes are trapped. In an online system, the thermal desorber is used to heat and provide inert gas flow, and

the analytes are trapped in the GERSTEL CIS 4 inlet liner. The analytes can be trapped cryogenically or on a sorbent. After analyte trapping is complete, the trap is rapidly heated to transfer the analytes onto the head of the GC column as a narrow band to provide optimum chromatographic performance. A sample size of 10-50 mg is typically used for this technique. The experimental variables that must be optimized are extraction temperature, extraction time, and flow rate across the sample. Since there is very little dilution (split) of the analytes before entering the GC column, this technique can provide very low detection limits, even with the relatively small sample size used.

The GERSTEL Twister® is an extraction device used for Stir Bar Sorptive Extraction (SBSE). The Twister enables ultra-trace determination of organic compounds in aqueous and gaseous matrices. It consists of a magnetic stir bar coated in glass with a PDMS sorbent layer. After sampling, the Twister is placed in an empty TD tube and heated in a thermal desorption system to release the analytes of interest.

This work shows optimized conditions for the determination of butylated hydroxytoluene (BHT) from a plastic bottle using DTE and from a saline solution using SBSE. Both samples were from a commercially available disposable enema product.

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### Experimental

#### Instrumentation

GERSTEL MPS LabWorks Platform, and Agilent 8890 GC/5977B Inert plus MSD. Figure 1 shows a picture of the system used for this study.



**Figure 1:** Picture of system used for this study.

#### Analysis Conditions LabWorks Platform

TDU 2	Splitless DTE: 40 °C (0 min); 300 °C/min; 250 °C (10 min) SBSE/Tenax®-TA: 40 °C (0 min); 300 °C/min; 280 °C (3 min)
CIS 4	Glass bead-filled liner Solvent venting 50 mL/min Split 20:1 -120 °C; 12 °C/s; 275 °C (3 min)

#### Analysis Conditions Agilent 8890 GC

Column	30 m HP-5 UI (Agilent) $d_i = 0.25$ mm, $d_f = 0.25$ $\mu$ m
Pneumatics	Constant Flow 1 mL/min
Oven	35 °C; 10 °C/min; 280 °C (2 min)

#### Analysis Conditions Agilent 5977B MSD

Mode	Scan
Scan	40-350 m/z

#### Sample Description

Disposable saline enema - Active ingredients: dibasic sodium phosphate and monobasic sodium phosphate. Inactive ingredients: benzalkonium chloride, disodium EDTA, and purified water. The saline volume was approximately 133 mL.

#### Sample Preparation

Direct Thermal Extraction - The saline solution was decanted from the plastic bottle into 40 mL VOA vials. The bottle was rinsed 3 times with DI water and allowed to dry. Approximately 20 mg samples were cut from the bottle and weighed into a TDU microvial. The microvials were placed into an empty TDU tube and capped with a transport adapter.

SBSE Analysis – Ten milliliters of saline solution was pipetted into a 10 mL screw cap vial. A Twister was added to the vial, and the sample was placed on a stir plate for 90 minutes at a speed of 1400 rpm. After extraction, the Twister was removed with forceps, rinsed in DI water, dried, and placed into an empty TDU vial. A transport adapter was placed on the tube.

#### Standard Preparation

Direct Thermal Extraction – Standards of BHT in methanol were prepared. One microliter of standard was spiked onto the fritted end of a TDU tube filled with Tenax®-TA. The tube was then attached to the GERSTEL Tube Spiking Apparatus, and dry nitrogen was run through the tube for 3 minutes at 50 mL/min. A transport adapter was then attached to the tube. A four-point calibration curve was prepared in the 2-1000 ng range on the tube.

SBSE Analysis – A one percent saline solution was prepared. Ten-milliliter aliquots of the saline solution were pipetted into 10 mL screw cap vials. BHT was spiked into the vials to prepare a 4-point calibration curve in the 2-200 ppb range.

#### Sample Introduction

Direct Thermal Extraction - The Tenax®-TA tubes were placed in a VT-40t tray on the autosampler. The standard was desorbed in splitless mode under a 50 mL/min helium flow @ 280 °C for 3.0 minutes. Analytes were trapped in the CIS inlet at -120 °C on a glass bead-filled liner. When desorption was complete, analytes were transferred to the column in split mode (20:1) by heating the inlet rapidly to 300 °C. The microvials with polymer samples were placed in a VT-40t tray on the autosampler. The standard was

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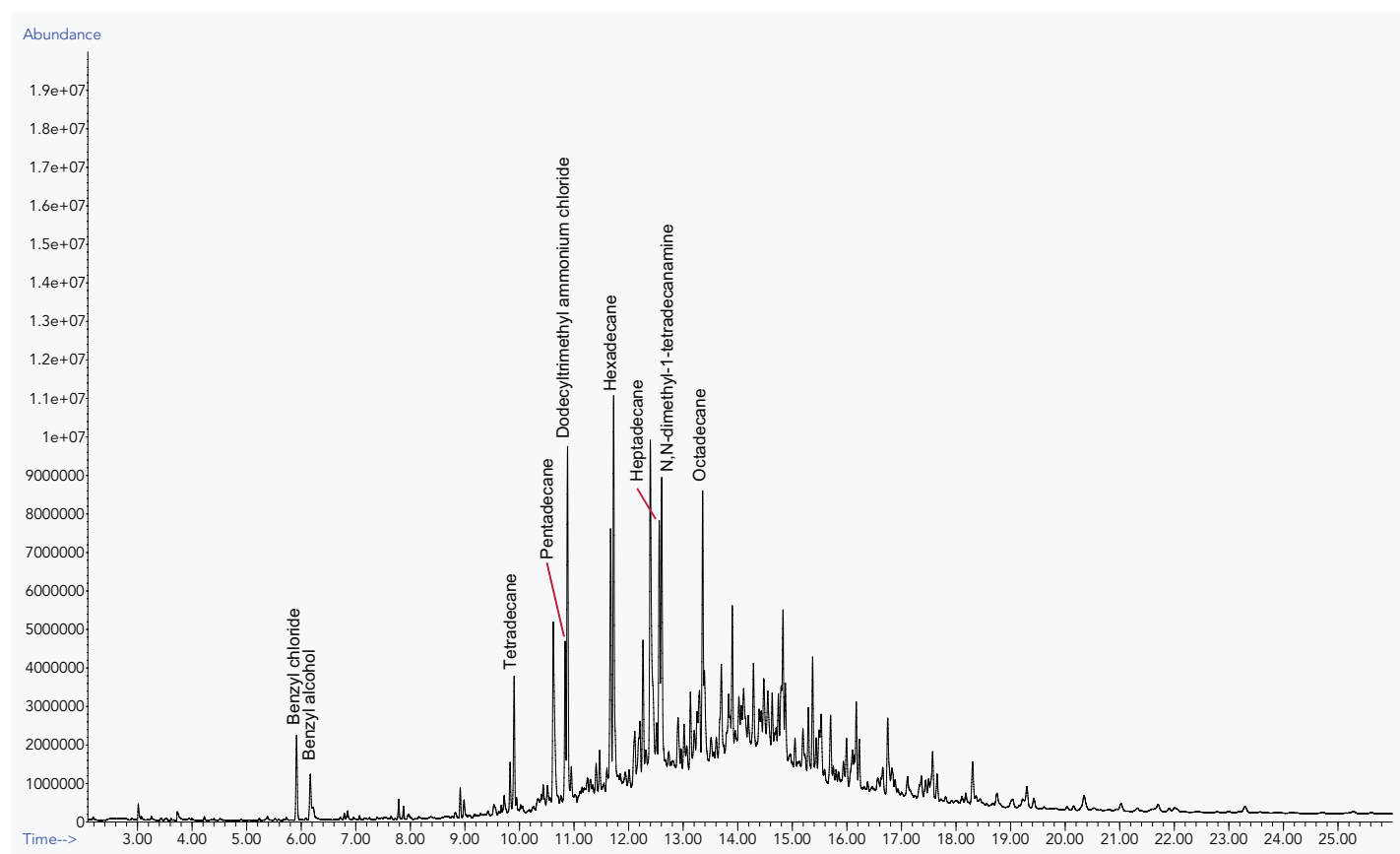
desorbed in splitless mode under a 50 mL/min helium flow @ 250 °C for 10.0 minutes. Analytes were trapped in the CIS inlet at -120 °C on a glass bead-filled liner. When desorption was complete, analytes were transferred to the column in split mode (20:1) by heating the inlet rapidly to 300 °C.

SBSE Analysis - The TDU tubes with Twisters were placed in a VT-40t tray on the autosampler. They were desorbed in splitless mode under a 50 mL/min helium flow @ 280 °C for 3.0 minutes. Analytes

were trapped in the CIS inlet at -120 °C on a glass bead liner. When desorption was complete, analytes were transferred to the column in split mode (20:1) by heating the inlet rapidly to 300 °C.

### Results and Discussion

A DTE analysis of the enema bottle is shown in Figure 2. An unresolved hydrocarbon hump, along with some alkanes and residual compounds from the saline solution, is seen in the chromatogram.

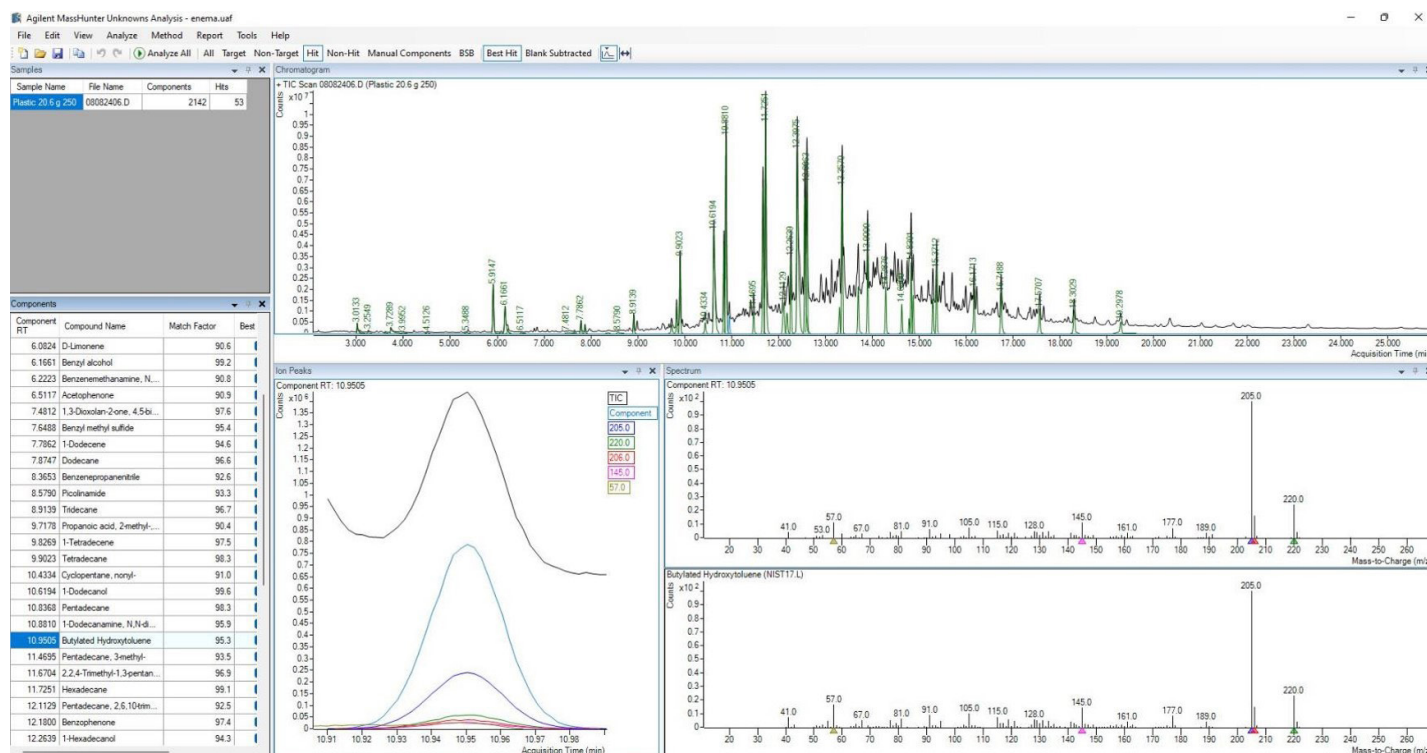


**Figure 2:** Total ion chromatogram for DTE extraction of plastic bottle.

To resolve the chromatogram, the file was run through Unknowns Analysis in the Agilent MassHunter software. Unknowns Analysis provides deconvolution, peak finding, and compound identification. Figure 3 shows the results for the DTE chromatogram. The results show the original and deconvoluted chromatograms along

with a components list. The peak at retention time 10.95 is identified as BHT. The match between the deconvoluted spectrum and the library match is shown in the results. The match quality is high at 95.3. BHT is a common antioxidant used in polymers.

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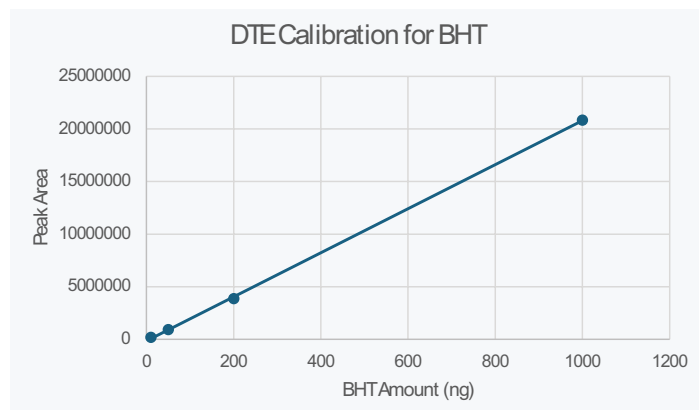
**Figure 3:** Unknowns analysis results for DTE extraction.

The optimized conditions for direct thermal extraction of the plastic enema bottle were found to be 250 °C for 10 minutes at a flow rate of 50 mL/min. Under these conditions, 96% of the BHT was extracted in the first analysis of the sample. This is based on three subsequent analyses of the same sample using the optimized conditions.

The calibration curve for the standards spiked onto Tenax®-TA is shown in Figure 4. Results for n=3 samples are shown in Table 1. The results show that BHT is present in the plastic bottle at a concentration of 8.41 ppm. The precision of the analysis is good, with a value of 5.0%.

**Table 1:** Quantitative data for DTE extraction of the plastic bottle.

Sample	Weight	Area	ng BHT	ppm BHT
1	0.0211	3498393	174	8.25
2	0.0224	3598294	179	7.98
3	0.0206	3729210	185	8.99
			Average	8.41
			RSD	5.0%



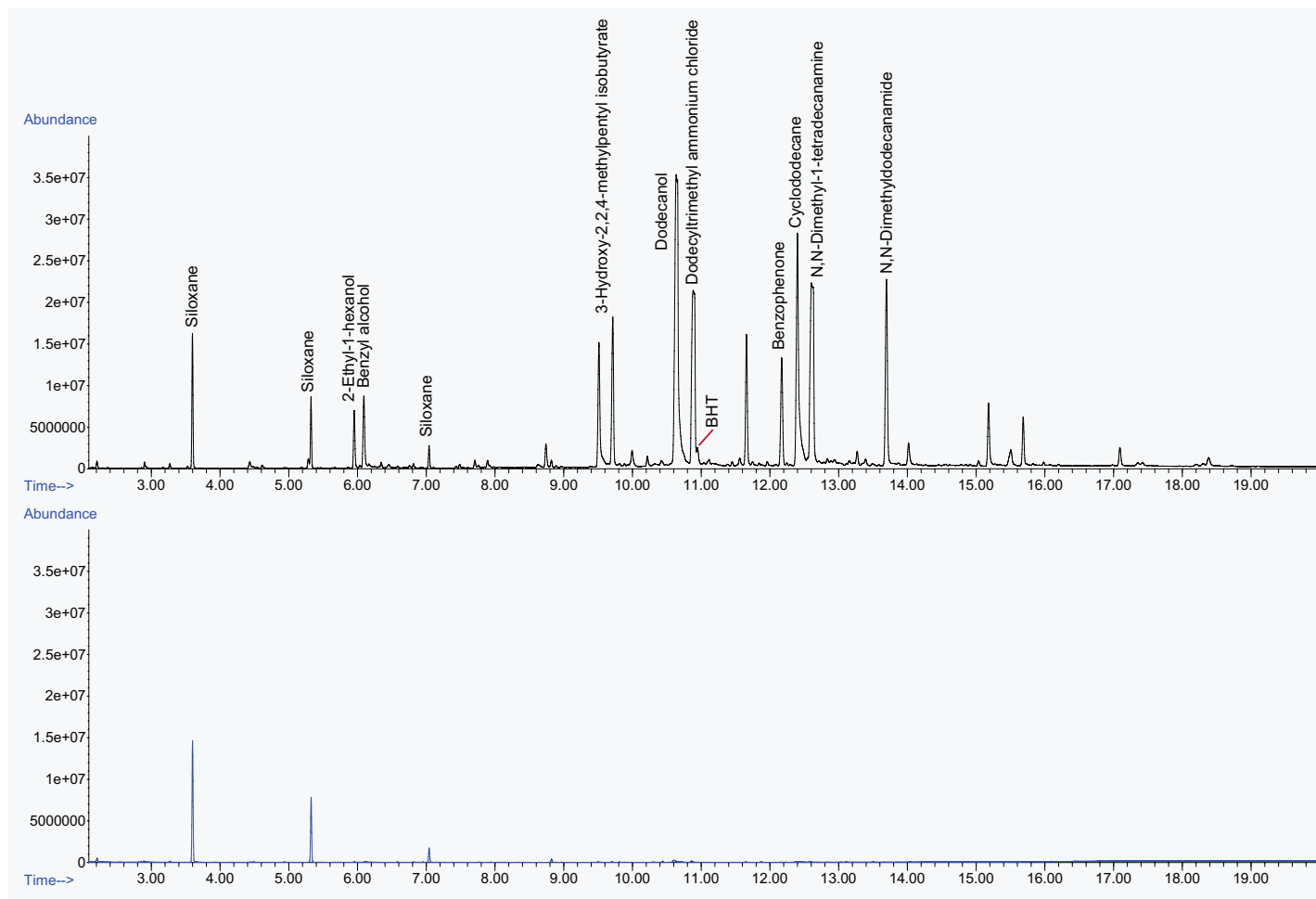
**Figure 4:** Calibration curve for DTE experiment.

The next step in the analysis was to see if the BHT had leached into the saline solution. SBSE was selected as the best extraction technique as it requires no solvent and results in a large concentration factor. The extraction efficiency for a compound can be estimated using the octanol-water partition coefficient ( $\text{Log } K_{o/w}$ ) for that compound. The Environmental Protection Agency provides a free download called EPI Suite™, which can be used to calculate the  $\text{Log } K_{o/w}$  for a compound (<https://www.epa.gov/ts-ca-screening-tools/download-epi-suite™-estimation-program-interface-v411>). The  $\text{Log } K_{o/w}$  for BHT was found to be 5.03. The recovery for Twister extraction is found using TwisterCalc software, available from GERSTEL. The estimated recovery for BHT using the standard 10 mm x 0.5 mm Twister is 99.6%. Therefore, Twister is an excellent choice for extracting BHT from this aqueous matrix.

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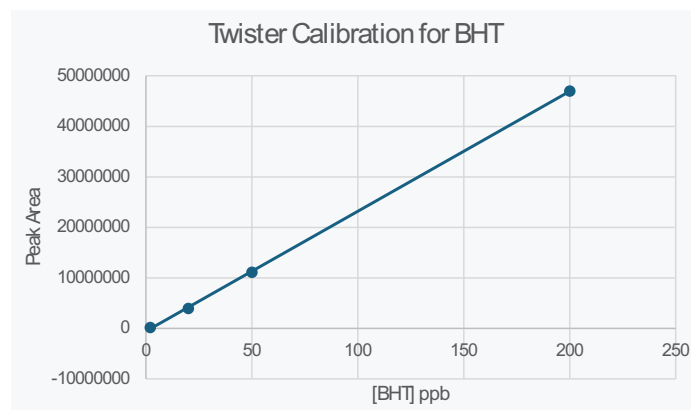
Figure 5 shows a stacked view of a Twister extract of the saline solution (top) and the same Twister run a second time (bottom). The BHT peak can be seen in full scan mode at a retention time of 11.0 min. Other matrix compounds are present as large peaks.

The lower chromatogram shows that the Twister and GC-MS system clean up quickly even though some of the other matrix peaks were very large.



**Figure 5:** Stacked view of Twister extract of enema saline solution (top) and redesorbed Twister (bottom).

The calibration curve for the matrix-matched saline standards is shown in Figure 6. Good linearity is seen for BHT between 2-200 ppb. Table 2 shows the quantitative data for n=3 samples of the saline solution from the enema bottle. The results show 46.5 ppb BHT in the saline product with good precision at 4.6%.



**Figure 6:** Calibration curve for SBSE experiment.

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**Table 2:** Quantitative data for SBSE extraction of the saline solution.

Sample	Area	[BHT] ppb
1	9962002	44.4
2	10298041	45.7
3	11171263	49.5
	Average	46.5
	RSD	4.6%

### Conclusion

This study demonstrates the use of direct thermal extraction and stir bar sorptive extraction for the determination of BHT in plastic and saline solutions, respectively. Both techniques require little sample preparation, use no solvent (green techniques), and provide low limits of determination with high precision, making them good choices for E&L studies.