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A Fully Automated Approach to the Analysis of NDMA in Water

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Introduction

N-Nitrosodimethylamine, or NDMA, can be formed during the treatment of drinking-water. Concentrations of NDMA in drinking-water have been measured up to 40 ng/litre, although lower concentrations are more common. NDMA is carcinogenic, and has been linked to the induction of tumours.

Within this application note, we show how SPE can be fully automated to enrich NDMA from water samples using ITSP cartridges. The injection of the NDMA extracts onto a GC/MS is also automated.

NDMA is a very polar molecule and is difficult to extract from water on most SPE phases. It has been found that coconut charcoal gives the best retention of NDMA and this stationary phase was chosen for this study.

Figure 1 shows the structure of NDMA.

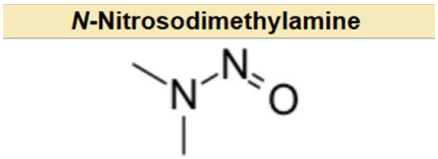

Figure 1 – Structure of NDMA

Figure 2 shows a photograph of the MultiPurpose Sampler (MPS) with Instrument Top Sample Preparation (ITSP).

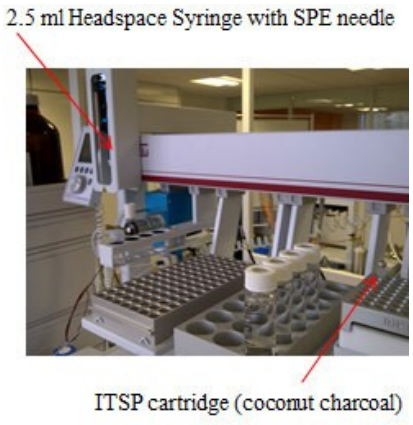

Figure 2 – MPS with ITSP

Figure 3 shows a photograph of a 25 mg coconut charcoal ITSP cartridge. The cartridges are approximately 3 cm in length.

Figure 3 – ITSP coconut charcoal cartridge

Instrumentation

GERSTEL MultiPurpose Sampler MPS 2 XL (Dual head)
Maestro Version 1.4.8.14/3.5
ITSP (Instrument Top Sample Preparation) Microliter
GERSTEL Cooled Injection System (CIS 4)
Agilent 5975 C inert XL MSD
Agilent GC 7890A

Method

A solution of 0.025 ng/ml NDMA and 0.04 ng/ml NDMA – d6 in water was prepared (Solution A).

A seven point calibration for NDMA was prepared in dichloromethane at concentrations ranging from 0.125 ng/ml to 4 ng/ml keeping the NDMA-d6 consistent at 1 ng/ml.

Extraction Procedure

Using the left MPS fitted with a 2.5 ml headspace syringe (SPE needle), the ITSP (coconut charcoal) cartridge was conditioned with 750 µl dichloromethane. 1000 µl of methanol was then loaded, followed by 2000 µl of HPLC grade water to equilibrate the cartridge. 10 ml of solution A containing NDMA was loaded and the cartridge was dried for 15 minutes with nitrogen using the headspace syringe. Drying is a critical step, to get the best recovery of NDMA and NDMA-d6 from the cartridge. After drying, 400 µl of dichloromethane is used to elute the NDMA and NDMA-d6 into a 2ml GC vial. The right MPS head fitted with

a 10 µl syringe is then used to inject 10 µl of the extract into the Cooled Injection System (CIS 4).

Solution A contains NDMA at 0.025 ng/ml. 10 ml of this solution was extracted. Therefore, assuming 100 % recovery, 0.25 ng NDMA will be enriched. Extracted NDMA from the ITSP cartridge is eluted in 400 µl. Therefore, the theoretical concentration of NDMA in the extract, is 0.625 ng/ml.

GC/MS Conditions

Large volume injection 10 µl (injection speed 1.18 µl/s)

CIS liner:Tenax
CIS 4:Temperature Program 10 °C (2 minutes);
12 °C/s to 250 °C (10 minutes)
Injection mode:PTV solvent vent for 2 minutes, followed by Splitless
GC column:DB-wax 30 m x 0.25 mm x 0.5 µm
Temp Program:50 °C ramped to 100 °C at 20 °C/minute (hold 1 minute) ramped to 240 °C (hold 1 minute)
MS:EI SIM 74 and 80 using lomass.u

Results

Table 1 shows the results obtained for the calibration points of NDMA and 3 separate extractions using ITSP.

Sample	NDMA M...	NDMA Results			NDMA-D6 (ISTD) Results	
Name	Exp. Conc	RT	Resp.	Final Conc.	Accuracy	Resp.
Blank		10.177	0	0.0000		10245
Cal 1	0.1250	10.661	1291	0.1061	84.9	10576
Cal 2	0.2500	10.654	2570	0.2404	96.1	9753
Cal 3	0.3750	10.654	4999	0.4456	118.8	10423
Cal 4	0.5000	10.647	6164	0.5364	107.3	10715
Cal 5	1.0000	10.654	11245	0.9973	99.7	10602
Cal 6	2.0000	10.654	20960	1.7610	88.1	11239
Cal 7	4.0000	10.654	41333	4.0375	100.9	9697
ITSP Blank		10.633	0	0.0000		4139
ITSP NDMA Extract 1		10.640	3239	0.6705		4520
ITSP NDMA Extract 2		10.640	2696	0.7073		3570
ITSP NDMA Extract 3		10.633	3401	0.6843		4652

Table 1 – Results for calibration points of NDMA and 3 separate extractions using ITSP

The amount (ng/ml) of NDMA found in three extracts was 0.6705, 0.7073 and 0.6843 respectively. The extract should contain 0.625 ng/ml. Therefore, recovery (with internal standard correction) can be calculated at 107 %, 113 %, and 109 % respectively. The mean recovery for has been calculated to be 110 %.

Without using the internal standard to correct, the recovery is approximately 40 %. However, the internal standard NDMA-d6 is recovered at the same amount as NDMA. Therefore, levels of NDMA can be accurately determined. You will notice the significant drop in response of NDMA-d6 in the extracts, from the internal standard areas in the last column of table 1.

Figure 4 shows the calibration plot for NDMA. A correlation coefficient of 0.996 was achieved.

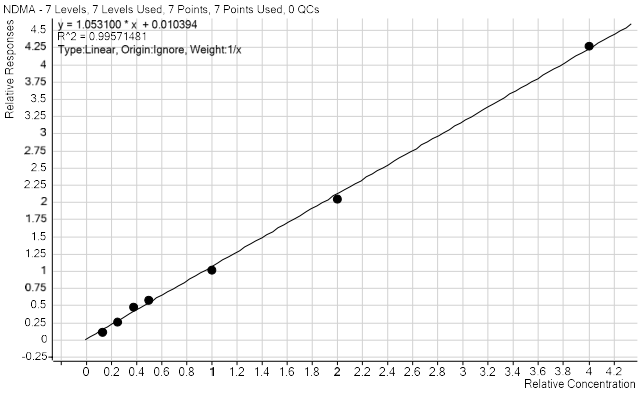

Figure 4 – Linearity plot of NDMA in dichloromethane

Figure 5 shows a SIM chromatogram of calibration level 1 (NDMA at 0.125 ng/ml)

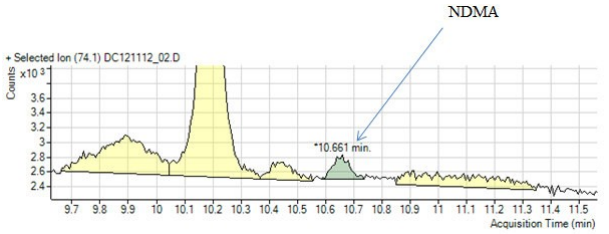

Figure 5 – SIM chromatogram of calibration level 1 (NDMA at 0.125 ng.ml)

Figure 6 shows a SIM chromatogram of sample extract 1 from ITSP (coconut charcoal).

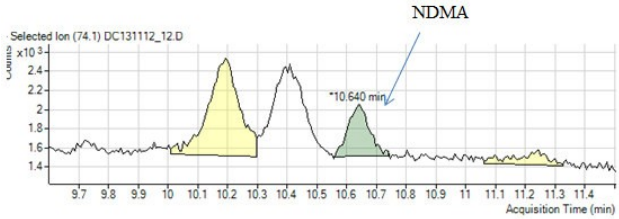

Figure 6 – Shows a SIM chromatogram of sample extract 1 from ITSP (coconut charcoal)

Discussion

This application notes shows how the extraction of NDMA from water samples can be fully automated using ITSP. The detection limit obtained on the single quadrupole instrument is at approximately 0.1 ng/ml.

For real sample analysis, a 7000 GC/MS/MS from Agilent operated in Multiple Reaction Monitoring mode will be used in conjunction with ITSP to get down to much lower detection limits for NDMA. The use of MS/MS should give much more specificity resulting in much cleaner chromatograms with little or no interfering peaks.

Anatune will have a 7000 GC/MS/MS installed at the end of December to start automating this method using the triple quadrupole instrument.

If you are interested in the automated extraction of NDMA from water, please contact Anatune.