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Nitrosamines in Formulations of Deet and EPTC

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N,N-diethyl-m-toluamide, commonly known as diethyltoluamide or deet, is a mosquito repellent for application on skin. It may be prepared by reacting m-toluacetyl chloride with diethylamine (DEA) in the presence of a base which could be an additional quantity of the secondary amine. S-ethyl dipropylthiocarbamate, also known as EPTC, is a pre- and post-emergent herbicide which is produced from the reaction of di-n-propylamine (DPA) with phosgene to give carbamyl chloride which then reacts with sodium ethyl mercaptide to give EPTC (Sitting 1980).

DEA and DPA are precursors of N-nitrosodiethylamine (NDEA) and N-nitrosodipropylamine (NDPA) respectively. Dimethylamine (DMA) has been reported to be contaminated with trace quantities of N-nitrosodimethylamine (NDMA) (Wigfield 1987a) which is carcinogenic to laboratory animals (Borzsonyi et al. 1978; Seiler 1977). If the secondary amines used to produce these pesticides are contaminated with nitrosamines, the contaminants may be carried over to the final products. In addition, two other pesticides, ferbam and dibam which are produced from DMA have been found to contain traces of NDMA (Wigfield unpublished). Thus deet and EPTC samples were chosen to be analysed for NDEA and NDPA respectively.

Several cleanup methods for low molecular weight volatile nitrosamines in pesticide formulations have been reported (Maybury et al. 1983; Wigfield et al. 1985). Most methods involve liquid-liquid extraction, column chromatography and solvent evaporation which are time consuming and labour intensive. The present paper describes the analysis of deet samples for NDEA and acetone solutions of EPTC for NDPA using a gas-liquid chromatograph coupled with a Thermal Energy Analyzer (GC-TEA)and bypassing any cleanup procedures, presents the results of the contaminants detected and discusses the usefulness of the method.

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MATERIALS AND METHODS

Standard NDEA in ethanol (95 ug/mL) was obtained from Thermedics and pure NDPA from Eastman Organic Chemicals.

Aliquots (2 uL) of deet or acetone solutions of EPTC (0.2 g/mL) alternating with NDEA (0.095 ug/mL) or NDPA (0.092 ug/mL) standard solutions in ethanol were injected into a Varian Vista 6000 gas-liquid chromatograph equipped with a Varian 8000 autosampler, a Varian Vista 402 data acquisition system and a TEA (model 543 Thermedics). The GC column (30 x 0.53 mm i.d. coated with 1.0 um DB 225) was connected to a 4-port post column switching valve with helical-drive air actuator and air solenoid. The valve was connected to either a TEA or flame ionization detector (FID) using deactivated fused silica tubing (1m x 0.53 mm i.d.) and was controlled by a Varian Vista 402.

The injection temperature was 160°C. Three sets of column temperatures were used: (1) 130°C for 2 min then 130-170°C at 20°C/min held at 170°C for 20 min for most deet samples, (2) 60-110°C at 8°C/min held at 110°C for 4 min for deet samples 1, 9 and 19 and (3) 130°C for EPTC samples. The helium flow rates were 15 mL/min for all samples and 3 mL/min for deet samples 1, 9 and 19. The switching valve was connected to TEA from injection time or 3 min before to 1 min after the nitrosamine response times to TEA. At all other times it was connected to a waste container and was purged by a separate helium gas at 3 mL/min. All other operating conditions were the same as described previously (Wigfield et al. 1987b). Under the given conditions, the response times of NDEA to TEA were 1.02 and 8.66 min and that of NDPA was 1.8 min.

Nitrosamines in samples were calculated using the following equation: NDEA (or NDPA) (ppm) = A/A' x W'/W x purity of standard, where A and A' = area response of sample and standard respectively; W' = weight of standard (ug) and W = weight of active ingredient (g) in 2 uL calculated from the label of the commercial product.

RESULTS AND DISCUSSION

As TEA detectors are selective to nitroso- or nitro-containing chemicals only, other chemicals injected into the detection system will, in principle, not interfere with the determination of nitrosamines. In practice, to maintain the sensitivity of the detector and to avoid contamination of the pyrolyzer tube and infrared filter, the extract injected into the system should be relatively free of large quantities of other chemicals.

In Canada, deet may be sold as technical material or formulated with ethanol or isopropanol (Sine 1988). The polarity and volatility of NDEA and alcohols render the isolation of NDEA from sample matrices using the conventional techniques practically impossible. However, because the solvent and deet are GC

compatible and assuming that other inert ingredients are also, the formulations may be injected directly into a GC-TEA system equipped with a post column switching valve. After column separation, the fraction containing NDEA could be directed to TEA for quantification and all other fractions to waste. Since NDEA is in trace quantities, it is desirable to elute NDEA before deet to avoid masking the NDEA response by the deet response. DB 225 GC column was found suitable for this purpose. Using the GC-FID detection system, NDEA and deet were eluted at 1.33 and 11.49 min. respectively (Figure 1a).

The results of NDEA in all 26 commercial deet samples are shown in Table 1. The identity of NDEA was confirmed by retention time comparison with a solution of its standard (Figures 1 b-c). The levels of NDEA in samples 13 and 16 were confirmed by standard addition method at four different spiking levels in the range of 0.2 to 1.25 ppm.

Table 1. NDEA (ppm)[1] in Deet (%) Samples Using GC-TEA Detection

Sample	NDEA	Deet[2]		Sample	NDEA	Deet	
1	ND[3]	14.25	P	21	ND	52.25	S
2	D[4]	95	L	22	ND	95	L
3	ND	19	S	23	ND	95	L
4	ND	95	L	24	ND	95	L
5	ND	52.2	S	25	D	95	L
6	ND	14.25	P	26	ND	95	L
7	ND	47.5	S				
8	ND	23.75	P				
9	ND	14.25	P				
10	ND	52.25	S				
11	ND	23.75	P				
12	ND	95	L				
13	0.05	23.75	P				
14	ND	95	L				
15	ND	38	P				
16	0.14	71.25	P				
17	ND	14.25	P				
18	ND	47.5	S				
19	ND	14.25	P				
20	ND	95	L				

(1) Average of duplicates, based on content of deet.

(2) Label concentration. P = pressurized, L = liquid, S = solution.

(3) ND = not detected with a detection limit of 0.02 ppm.

(4) D = detected below a quantitation limit of 0.05 ppm.

To test the usefulness of this analytical technique, six samples of EPTC were analysed for NDPA using the same technique, with results shown in Table 2 and the analyte response to FID and TEA detectors in Figures 1 d-f.

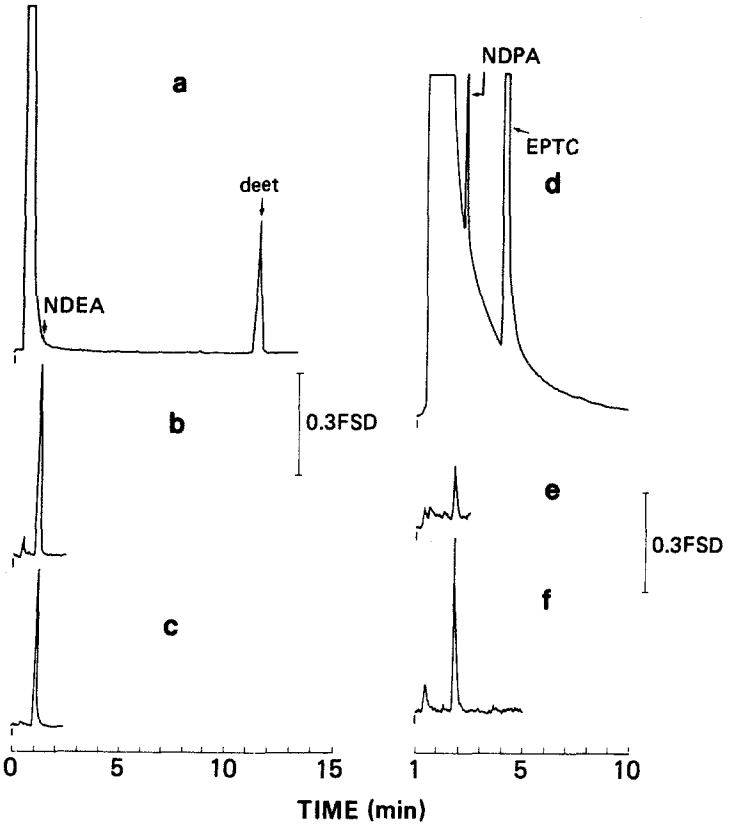

Figure 1. Typical GC chromatograms: (a) FID response to deet sample 22 spiked with NDEA (0.1 ppm), (b) TEA response to NDEA in deet sample 16, (c) TEA response to NDEA standard (0.38 ng), (d) FID response to EPTC sample 6 spiked with NDPA (1.55%), (e) TEA response to NDPA in EPTC sample 4 and (f) TEA response to NDPA standard (18 pg). FSD = Full scale deflection.

The recoveries of NDEA in spiked deet samples are shown in Table 3. Using standard statistical calculation, the overall mean NDEA recovery, standard deviation (SD) and coefficient of variation (CV) were 97.8, 8.7 and 8.9% respectively. The responses of the TEA to a series of NDEA standards were linear over a range of 38 pg to 1.9 ng. The limit of detection (LOD), defined as 3 x SD (n = 6) at 0.019 ppm, was 0.02 ppm and the limit of quantitation (LOQ), defined as 10 x SD, was 0.05 ppm. These data indicate that the method has good precision and accuracy.

Table 2. NDPA (ppm)[1] in EPTC Samples[2] Using GC-TEA Detection

Sample	NDPA
1	0.05
2	0.10
3	0.11
4	0.36
5	0.25
6	0.09

(1) Average of duplicates, based on content of EPTC.

(2) Formulated as emulsifiable concentrate in 800 g/L.

Table 3. Recoveries of NDEA from Fortified Deet Formulations Using GC-TEA

Deet No.	NDMA (ppm) Present(A)	Fortified(B)	Found(C)	Recovery (%) (C-A)/B X 100
13	0.05	0.25	0.27	96
		0.22	0.27	100
		0.67	0.73	101
		0.66	0.73	103
	0.07	0.83	0.80	88
		0.84	1.03	114
16	0.15	0.27	0.4	93
		0.26	0.39	96
	0.16	0.66	0.85	104
		0.64	0.75	92
	0.15	0.89	1.09	105
		1.06	1.21	100
	0.16	1.22	1.37	100
		1.28	1.15	77
mean recovery				97.8
SD (n = 14)				8.7
CV (n = 14)				8.9

The recoveries of NDPA in spiked EPTC samples are shown in Table 4. Using a similar calculation at 0.07 ppm spike level (n = 6), the LOD was 0.04 ppm and the LOQ was 0.12 ppm.

This work shows that a GC post column switching valve coupled with a TEA detector is useful for determining trace quantities of nitrosamines in a mixture of GC compatible chemicals. NDEA was detected in four deet samples at 0.02 - 0.14 ppm and NDPA in all six EPTC samples at 0.05 - 0.36 ppm.

Table 4. Recoveries of NDPA from Fortified EPTC Sample 1 Using GC-TEA

NDPA (ppm) Present(A)	Fortified(B)	Found(C)	Recovery (%) (C-A)/B X 100
0.05	0.22	0.27	100
	0.23	0.26	93
	0.24	0.28	96
		0.27	92
		0.27	92
		0.30	100
mean recovery			96.1
SD (n = 6)			3.8
CV (n = 6)			2.5

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