Determination of Daminozide and Dimethylhydrazine Residues in Swiss Apple Juice Concentrates Using Gas Chromatography–Mass Spectrometry

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Apple juice concentrates analyzed for daminozide and 1,1-dimethylhydrazine (UDMH) by a sensitive gas chromatographic mass spectrometric (GC–MS) method showed with the exception of one sample no detectable concentrations of daminozide. The exceptive sample showed traces of daminozide (0.07 ppm) that could have resulted from the illegal use of daminozide by one fruit grower from more than a hundred. The samples were collected from large-scale storage tanks in different regions in Switzerland and represented a cross section of Swiss production. The samples were analyzed for daminozide after alkaline digestion to UDMH and derivatization to pentafluorobenzoyl derivatives. The exceptive apple juice concentrate was further analyzed directly for UDMH by isolation via cation-exchange chromatography and derivatization. No UDMH was found in this analysis. Comparative analysis showed the GC–MS method to be much less susceptible to interfering compounds than electron capture detection. Other hydrazines were comparatively analyzed and GC and MS properties of the pentafluorobenzoyl derivatives reported.

INTRODUCTION

Daminozide (Alar; succinic acid 2,2-dimethylhydrazide) is a plant growth regulator used to improve the harvest quality of several fruits and vegetables. Since registered in 1963, it has been primarily used on apples to control induction of flowering, prevent spoilage and watercore development, reduce fruit drop, and improve color development and storage properties (Dozier et al., 1985). Persistence of daminozide with significant residues has been observed in apples that outlast the preharvest intervals of 60–70 days recommended in the United States (Edgerton and Greenhalgh, 1966; Edgerton et al., 1967).

Daminozide has been identified as a possible carcinogen in laboratory animals (Toth et al., 1977). Studies on daminozide degradation have shown partial hydrolysis of daminozide to 1,1-dimethylhydrazine (unsymmetrical dimethylhydrazine, UDMH) in apples and apple products that are subsequently boiled (Newsome, 1980; Hurter et al., 1989; Saxton et al., 1989). UDMH itself has been identified as a toxin (Barth et al., 1976; Chevrier and Pfister, 1974) and as a potential carcinogen in studies with laboratory animals, and residues have been recognized as a potential human health risk when present in foods (Kimura et al., 1984; Sakita et al., 1983; Christenson and Luginbyhl, 1975; Roe et al., 1967).

The available methods for determining daminozide are based on its hydrolysis in strong alkali and the recovery of UDMH released by distillation (Newsome, 1980; Saxton et al., 1989). Derivatization of UDMH with pentafluorobenzoyl chloride (PFB-Cl) yields 1,1-dimethyl-2,2-bis(pentafluorobenzoyl)hydrazine [UDMH-bis(PFB)]. The reaction mixture was further purified on silica, and the derivatives were quantified by gas chromatography with electron capture detection (GC–ECD).

UDMH formed from daminozide in apple products during various processing steps can be directly analyzed by isolation of UDMH via cation-exchange chromatography followed by derivatization, clean up, and GC–ECD analysis (Newsome, 1980). Derivatization methods involving PFB-Cl can cause interference in ECD as a number of other PFB derivatives are formed from various compounds in samples and reagents, thus giving false-positive results.

In Switzerland, evidence concerning the degradation of daminozide to UDMH led in 1986 to the suspension of its use as a plant growth regulator in fruit production (Hurter et al., 1989). However, the compound is still registered for use in the production of ornamental plants.

In the spring of 1989 public concern in the United States was focused on the potential risk of daminozide residues in foods, especially in processed apple products for infants (Roberts, 1989).

The present study was initiated 3 years after the suspension of daminozide in Switzerland. Several samples of apple juice concentrates from various locations were analyzed for the presence of daminozide and its degradation product UDMH. Other hydrazines were derivatized and analyzed for comparison.

EXPERIMENTAL PROCEDURES

Apple Juice Concentrates. Six samples of apple juice concentrate (harvest 1988) were collected from two bulk storage tanks (50 000 L) each from three processors located in central, western, and eastern Switzerland and produced from apples of many individual growers. All samples (H51, H53, G105, G106, T240, T243) were collected between March and April 1989 and were stored (1–2 months) at 4 °C until analyzed. An additional sample of apple juice concentrate (M) produced at the Swiss Federal Research Station in Wädenswil (Switzerland) was used as control.

Materials. UDMH, 1,2-dimethylhydrazine (symmetrical dimethylhydrazine, SDMH), methylhydrazine, and hydrazine were obtained from Fluka AG, Buchs, Switzerland. Daminozide was provided by J. Hurter (Federal Research Station, Wädenswil). Cation-exchange resin, Dowex 50W X8, 100–200 mesh, was purchased from Sigma Chemie GmbH, Deisenhofen, FRG. Before use, the resin was washed with alkali and acid according to the method of Newsome (1980).

Determination of Daminozide as UDMH. Samples of 5 g of apple juice concentrate were hydrolyzed in strong alkali (50% NaOH), and the released UDMH was recovered by distillation (Newsome, 1980). To 10 mL of distillate, 0.1 mL of concentrated HCl was added and 1-mL aliquots were derivatized by adding

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Table I. GC and EI MS Data of PFB Derivatives of Hydrazine, Methylhydrazine, UDMH, and SDMH

compound	E_T,[a] °C	EI data m/z[b]
hydrazine-tetrakis(PFB)	228	808 (0.27), 597 (0.49), 402 (0.7), 195 (100), 167 (16)
hydrazine-bis(PFB)	170	420 (0.7), 405 (0.22), 265 (0.012), 195 (100), 167 (23)
methylhydrazine-tris(PFB)	212	628 (0.1), 417 (12), 195 (100), 167 (23)
methylhydrazine-bis(PFB)	185	434 (0.73), 406 (0.19), 195 (100), 167 (18)
UDMH-bis(PFB)	158	448 (7), 253 (73), 195 (100), 181 (11), 167 (19)
SDMH-bis(PFB)	184	448 (7), 420 (11), 253 (10), 195 (100), 167 (18)

[a] E_T, elution temperature. [b] Characteristic ions, relative intensities given in parentheses; M^+ ions underlined.

9 mL of 2 M K_2CO_3 and 1 mL of PFB-Cl reagent (0.1 mL of PFB-Cl dissolved in 10 mL of dichloromethane). The reaction mixture was then shaken vigorously for 1 h. After extraction with two 5-mL portions of dichloromethane, the combined extracts were dried over a bed of sodium sulfate and further chromatographed on a small column of 0.5 g of silica gel (70–230 mesh; Merck, Darmstadt, FRG) and 0.5 g of sodium sulfate in a 140 × 6 mm disposable Pasteur pipet. The column was washed with a total of 5 mL of additional dichloromethane. The eluates were then concentrated in a stream of nitrogen and the residues redissolved in 500 μL of toluene prior to GC–MS analysis. The quantity of UDMH determined included any free UDMH present prior to the hydrolysis of daminozide and was expressed as "total" UDMH. Recovery experiments were carried out by adding known quantities of daminozide (0.1–5 ppm) and UDMH (0.01–1 ppm) to selected apple juice concentrates, followed by hydrolysis, distillation, and derivatization.

Direct Determination of UDMH. UDMH in apple juice concentrates was isolated by cation-exchange chromatography according to the method of Newsome (1980). Aliquots of 1 mL of eluate were then subjected to derivatization with PFB-Cl as described for daminozide and analyzed as "free" UDMH by GC–MS. For recovery studies, apple juice concentrates were fortified with UDMH in the range 0.01–1 ppm.

Reference Compounds. Standard solutions of UDMH, SDMH, methylhydrazine, and hydrazine were prepared at concentrations of 10 μg/mL in 0.01 M HCl. Aliquots of these solutions were derivatized with PFB-Cl and analyzed by GC–MS to detect and identify the corresponding PFB derivatives.

Standard solutions of UDMH were also used as external standards (linearity of derivatization; quantification) and for fortification of the apple juice concentrates in the range 0.01–1 ppm. A standard solution of daminozide (10 μg/mL in 0.01 M HCl) was used in fortifying apple juice concentrates at 0.1–5 ppm. In some analyses SDMH was used as internal standard.

GC–MS Analysis. A Finnigan 4023 instrument operating in the electron-impact mode (EI, 70 eV) and a 25-m SE 54 fused silica (0.32 mm i.d.) capillary column were used. The column was temperature programmed as follows: 80 °C isothermal for 2 min, to 100 °C at 20 °C/min, and then to 280 °C at 5 °C/min. Aliquots of 1–2 μL of sample were injected. Full-scan EI mass spectra (m/z 35–835, 1 s/scan) were recorded for peak identification. Quantification of UDMH and SDMH was carried out by selected ion monitoring (SIM) using the molecular ion (M^+) at m/z 448 and fragment ions at m/z 181 (only for UDMH), 195, and 253 (0.5 s/scan) (for relative ion abundance, see Figure 1 and Table I). In this mode, the minimal detectable quantity of UDMH using m/z 448 was 2–4 pg, corresponding to 0.5–1 ng in the derivatized aliquot and to a concentration of 0.01 ppm of UDMH in apple juice concentrate.

GC–ECD Analysis. In addition to GC–MS, the samples were analyzed by GC–ECD for comparison. In this case an additional cleanup step was required. After dichloromethane was removed under a stream of nitrogen (compare Determination of Daminozide as UDMH), the PFB derivatives were redissolved in 2 mL of n-hexane and loaded onto a 6 mL/1 g Chromabond SiOH cartridge (Macherey-Nagel, Oensingen, Switzerland). The PFB derivatives were then eluted from the cartridge with 10 mL of toluene–n-hexane (15:85 v/v).

A 25-m SE 54 fused silica column and a Carlo Erba HRGC 5300 Mega series gas chromatograph with ECD was used. Aliquots of 1 μL were injected with a split ratio of 1:10 at 80 °C. The column temperature was isothermal at 80 °C for 2 min, programmed to 140 °C at 10 °C/min, to 220 °C at 5 °C/min, and to 250 °C at 20 °C/min. For confirmation of the UDMH-bis-(PFB) derivative in the GC analysis with ECD, standards of 100 μg and 100 ng UDMH/mL in 0.01 M HCl were prepared and derivatized as previously described. An injection of 20 pg of UDMH as bis derivative (corresponding to about 1 ppm of daminozide in apple juice concentrate) resulted in a peak with 80% full-scale deflection under the operating conditions.

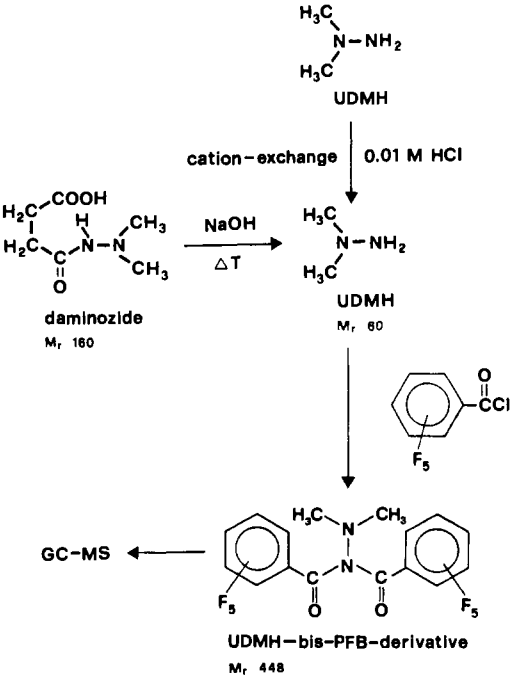

Figure 1. Analytical scheme for daminozide and UDMH. M_r, molecular weight.

RESULTS AND DISCUSSION

Analytical Scheme and General Considerations. Daminozide is too polar to allow direct GC–MS analysis. As in most previous studies, its conversion to UDMH under alkaline reflux conditions was used (see scheme, Figure 1). UDMH is then derivatized by using pentafluorobenzoyl chloride (PFB-Cl). The resulting derivative is sufficiently stable to allow GC and GC–MS analysis. The analytical scheme described by Newsome (1980) was used with minor modifications. In addition, direct analysis of free UDMH was carried out by using a slightly modified procedure of Newsome (1980).

GC and MS Properties of PFB Derivatives of Hydrazines. The derivatization of the various hydrazines using pentafluorobenzoyl chloride was investigated by using EI GC–MS. The mass spectra (see Figure 2) indicate the formation of a tetrakis derivative from hydrazine (M^+, m/z 808), a tris derivative from methylhydrazine (M^+, m/z 628), and bis derivatives from both dimethylhydrazines (M^+, m/z 448) as major products. This indicates that all amino/imino hydrogens in these hydrazines react with the PFB-Cl reagent. The EI mass spectra show the presence of molecular ions (M^+) and fragment ions. Some fragment ions apparently are formed by simple cleavage of the C–N amide bonds (loss of COC_6F_5 to $M^+ - 195$).

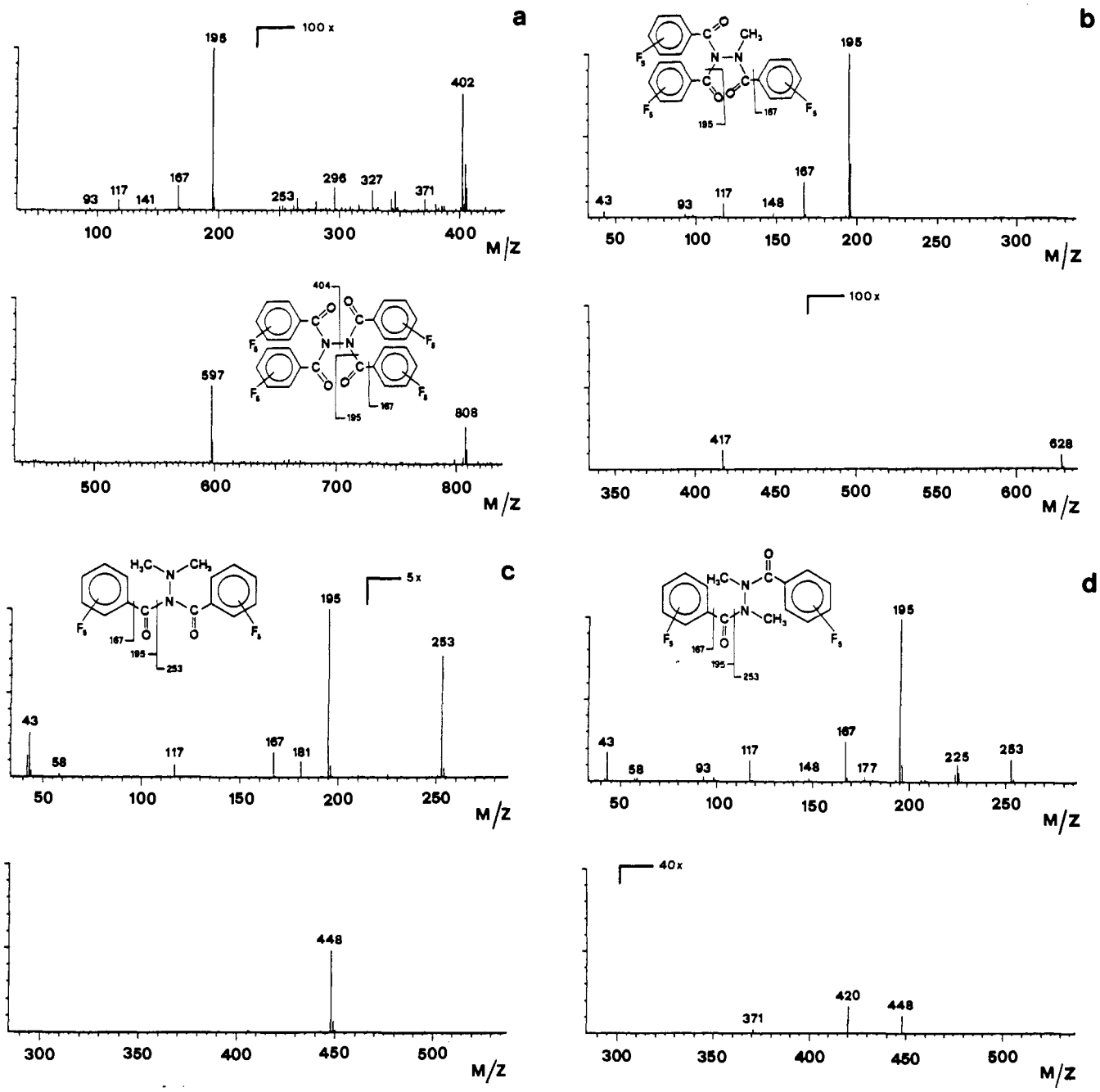

Figure 2. Mass spectra (EI) of the PFB derivatives of hydrazine (a), methylhydrazine (b), UDMH (c), and SDMH (d).

Others are formed via more complex rearrangement reactions. All four derivatives show a base peak at m/z 195 (pentafluorobenzoyl cation); additional ions are formed by subsequent fragmentation of this ion.

The elution temperatures and retention times (see Table I) increase with increasing molecular weight of the derivatives. However, a large difference in the retention time was observed between the two isomeric dimethylhydrazine-bis(PFB) derivatives. The more linear derivative of SDMH is eluted at 184 °C, higher than the derivative of UDMH (158 °C). Small amounts of incomplete derivatized products were only observed for methylhydrazine and hydrazine, but not for the dimethylhydrazines: a bis derivative was observed from methylhydrazine (M^+, m/z 434; 1% yield) and from hydrazine (M^+, m/z 420; 5–10% yield). The mono derivatives of methylhydrazine and hydrazine, and the tris derivative of hydrazine, however, were not observed. From the retention data and structural considerations of the bis derivatives of hydrazine and methylhydrazine the formation of the linear 1,2 derivatives was presumed. This would indicate that derivatization of primary amino groups in hydrazines are favored over secondary amino or amide groups.

Analysis of UDMH-bis(PFB) by SIM–GC–MS. Derivatization of UDMH was investigated in detail by reacting various amounts (0–10 000 ng) under different reaction conditions. The results indicated that the bis derivative of UDMH is formed rather quickly and that the reaction reaches completion within minutes. Linearity of the SIM–GC–MS response (r^2 = 0.994, n = 7) was observed in the range 0–330 ng of UDMH reacted (0–660 pg injected) corresponding to 0–0.66 ppm of UDMH in apple juice concentrates analyzed according to the procedure of Newsome (1980). A GC–MS detection limit of 2–4 pg using the m/z 448 ion and 1 pg using the m/z 253 ion was observed; the more intense m/z 195 ion was not

Table II. GC-MS Analysis of UDMH-bis(PFB) Derivative in Apple Juice Concentrates Fortified with Daminozide and UDMH

sample	apple juice concentrate	fortification	$UDMH_{total}$ (distillation) ng	ppm	recovery %
1	M	none	nd	<0.002	-
2		0.01 ppm of UDMH	1.2	0.0024	24
3		0.1 ppm of UDMH	18	0.036	36
4		1 ppm of UDMH	585	1.17	117
5	H51	none	nd	<0.002	
6		0.1 ppm of daminozide	7	0.014	38[a]
7		1 ppm of daminozide	172	0.34	92[a]
8		5 ppm of daminozide	982	1.96	105[a]

sample	apple juice concentrate	fortification	$UDMH_{free}$ (cation exchange) ng	ppm	recovery %
9	G106	none	nd	<0.001	-
10		0.01 ppm of UDMH	0.5	0.001	10
11		0.1 ppm of UDMH	11	0.022	22
12		1 ppm of UDMH	500	1	100

[a] Converted to daminozide (conversion factor 2.7).

Table III. Determination of Daminozide as UDMH-bis(PFB) Derivative in Apple Juice Concentrates from Central, Western, and Eastern Switzerland

apple juice concentrate	GC-MS analysis of UDMH-bis(PFB) derivative ng	ppm
H51	nd[a]	<0.002
H53	12.5	0.025[b,c]
G105	nd	<0.002
G106	nd	<0.002
T240	nd	<0.002
T243	nd	<0.002
M (control)	nd	<0.002

[a] nd = <1 ng. [b] 0.025 ppm of UDMH corresponds to 0.07 ppm of daminozide (conversion factor 2.7). [c] Samples H53 was additionally analyzed for UDMH directly and found to be negative (<0.001 ppm).

sufficiently selective. The ion at m/z 195 is common to any PFB derivative.

Determination of Daminozide as UDMH in Apple Juice Concentrates. Six samples of apple juice concentrate and the control sample (5-g aliquots) were analyzed for daminozide. The control sample and several of the other samples (determined as daminozide negative) were additionally fortified with known amounts of daminozide (0.5–25 μg, corresponding to 0.1–5 ppm) or 0.05–5 μg of UDMH (0.01–1 ppm in apple juice concentrate) prior to alkaline digestion and distillation. The results are listed in Table II. They indicate recoveries in the range 38–105% for daminozide and 24–100% for UDMH. The lower recoveries in the range 24–38% were observed from samples with fortifications of 0.01 and 0.1 ppm of UDMH and 0.1 ppm of daminozide, respectively. They could be caused by losses of the highly volatile UDMH during digestion of daminozide and distillation. Losses of UDMH appear to be higher in fortifications with UDMH than with daminozide. The results show almost complete conversion of daminozide into UDMH (theoretical conversion factor of 2.7, ratio of molecular weights of daminozide/UDMH). The detection limit was 0.01 ppm.

The results of the analysis of apple juice concentrates for daminozide are presented in Table III. They show with the exception of one sample no detectable concentrations of daminozide or UDMH (<0.01 ppm). The analysis of sample H53 indicated a concentration of 0.025 ppm of UDMH corresponding to 0.07 ppm of daminozide. The amount of 0.07 ppm of daminozide in sample H53 could result from the illegal use of the plant growth regulator by a single fruit grower from more than 100 growers where expected residues of daminozide in apples correspond to 1–3 ppm at harvest and 6–20 ppm in concentrate when derived from such a treatment.

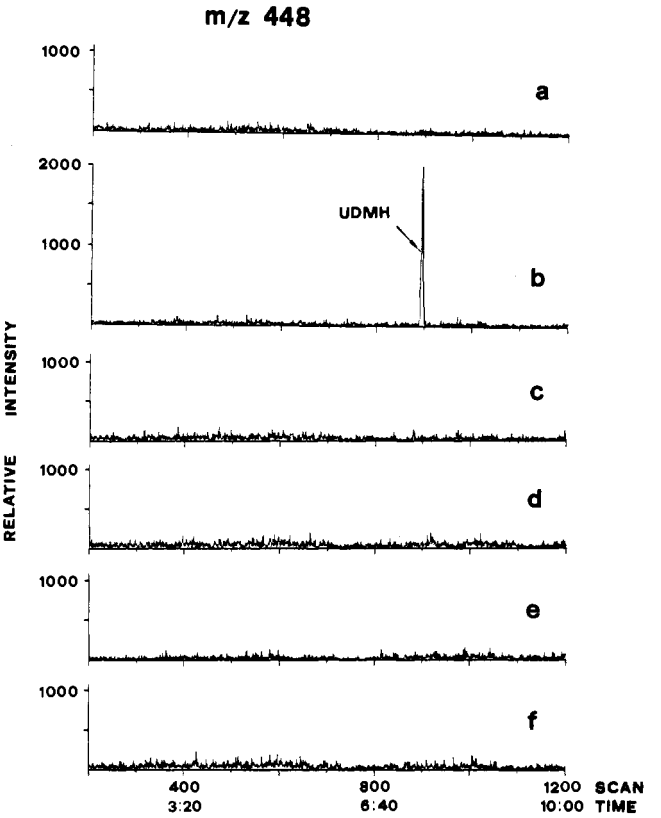

Figure 3. Mass chromatograms (EI, m/z 448) of Swiss apple juice concentrates analyzed for daminozide as UDMH-bis(PFB). Apple juice concentrates: (a) H51; (b) H53; (c) G105; (d) G106; (e) T240; (f) T243. For analytical procedure and GC-MS conditions, see the text.

Mass chromatograms (m/z 448) of analyzed samples are presented in Figure 3. The presence of daminozide as UDMH in sample H53 (Figure 3b) was indicated from the signal at m/z 448 (M^+) and further confirmed by the simultaneous signals at m/z 448, 253, 195, and 181 (Figure 4) in correct intensity ratios and at the correct retention time of the UDMH-bis derivative. The quantity of UDMH-bis(PFB) actually detected in sample H53 (around 25 pg) was too small to allow recording of a complete mass spectrum.

The use of a surrogate compound (internal standard) was investigated by using the isomeric SDMH. Analysis of apple juice samples first showed the complete absence of SDMH (<0.01 ppm). Aliquots of the apple juice concentrate G105 were further fortified with different concentrations of daminozide (0.1–5 ppm) and 1 ppm of SDMH. The results are presented in Table IV. Recovery of SDMH was acceptable, yielding, however, values slightly different from those obtained for UDMH. SDMH and UDMH, therefore, seem to behave differently during digestion, cleanup, and derivatization. As such, SDMH cannot be used as an ideal surrogate compound for UDMH but can nevertheless be applied as a control in sample preparation and derivatization and possibly improves quantitation in the GC–MS analysis. Stable-isotope-labeled UDMH (e.g., 2D6-UDMH), which could be used

Table IV. GC-MS Analysis of UDMH-bis(PFB) Derivative in Apple Juice Concentrate (G105) Fortified with Daminozide and 1,2-Dimethylhydrazine (SDMH) as Internal Standard

	GC-MS Analysis of UDMH/SDMH-bis(PFB) derivative					
	$UDMH_{total}$ (distillation)			$SDMH_{total}$ (distillation)		
fortification	ng	ppm	recovery %	ng	ppm	recovery %
none	nd[a]	<0.002		nd[d]	<0.01	-
1 ppm of daminozide	155	0.31	84[c]	-	-	-
1 ppm of SDMH	-	-	-	390	0.78	78
0.1 ppm of daminozide/1 ppm of SDMH	10 (10)[b]	0.02 (0.02)	54 (54)[c]	505	1.01	101
1.0 ppm of daminozide/1 ppm of SDMH	159 (215)	0.32 (0.43)	86 (116)[c]	370	0.74	74
5.0 ppm of daminozide/1 ppm of SDMH	805 (930)	1.62 (1.89)	87 (102)[c]	425	0.85	85

[a] nd = <1 ng (compare Table II). [b] Values in parentheses were calculated with SDMH as internal standard (IS). [c] Expressed as daminozide (conversion factor 2.7). [d] Estimated detection limit about 1–5 ng.

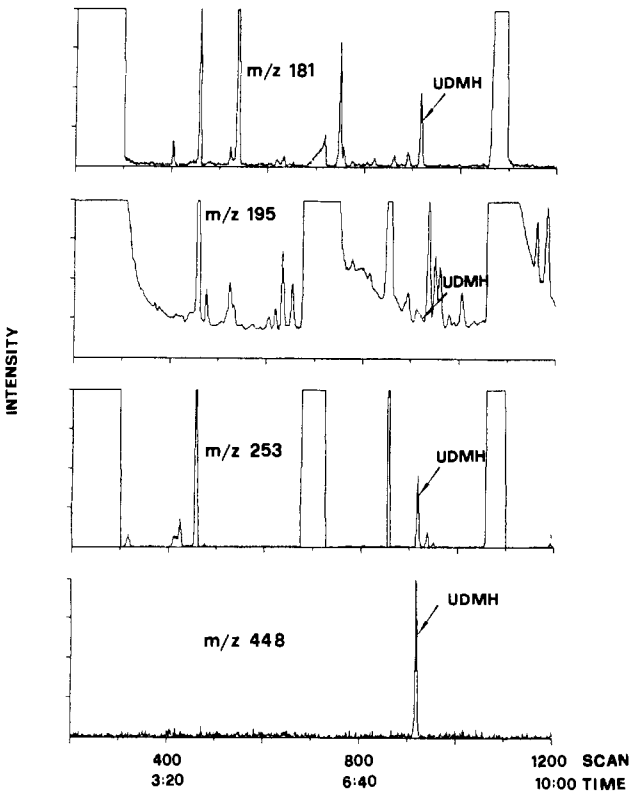

Figure 4. Mass chromatogram (*m/z* 181, 195, 253, and 448) of UDMH-bis(PFB) derivative confirming the presence of daminozide in apple juice concentrate H53. For analytical procedure and GC-MS conditions, see the text.

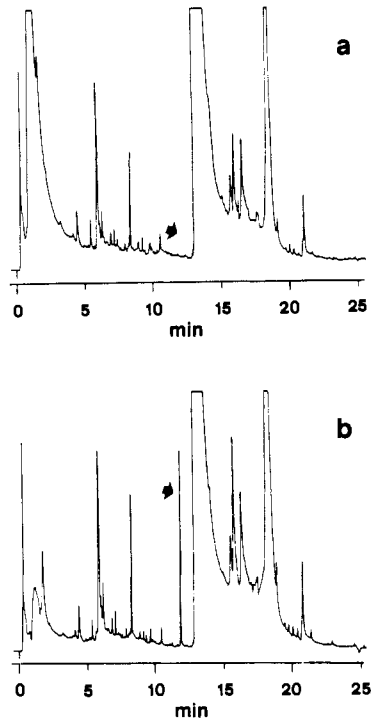

Figure 5. ECD chromatograms of apple juice concentrate H51 analyzed for daminozide as UDMH showing (a) the absence of UDMH-bis(PFB) derivative in derivatized sample and (b) the presence of UDMH-bis(PFB) derivative in derivatized sample fortified with 1 ppm of daminozide. For analytical procedure and GC-ECD analysis, see the text.

as an ideal surrogate compound and internal standard, is presently not available.

Direct Analysis of UDMH in Apple Juice Concentrates. Daminozide has been determined by its degradation to UDMH and subsequent derivatization of the latter. It was unsure whether UDMH was formed by degradation or whether UDMH was present as such in free form. Therefore, apple juice concentrate H53 was directly analyzed for UDMH by isolation via chromatography on a cation-exchange resin and derivatization with PFB-Cl according to the method of Newsome (1980). Sample H53, positive for UDMH after digestion, showed no measurable concentration of UDMH when analyzed for free UDMH (see Table III), indicating that H53 was contaminated with trace amounts of daminozide.

Samples of apple juice concentrate G106 were further fortified with various concentrations of UDMH (0–1 ppm) and directly analyzed for UDMH (Table II). Detection limits for the determination of UDMH in apple juice concentrate via cation-exchange chromatography were 0.01 ppm. Although in the concentration range 0.01–0.1 ppm recovery was low (10–22%), detection and quantitation of UDMH were possible. The recovery was nearly 100% at fortifications of 1 ppm of UDMH and higher. Low recoveries might be caused by irreversible adsorption of UDMH on the ion-exchange resin or degradation (oxidation).

GC-ECD Analysis and Comparison to GC-MS Analysis. ECD (electron capture detection) is a more available analytical technique. Figure 5 shows ECD chromatograms of a typical derivatized sample of apple juice concentrate (H51) with and without addition of 1 ppm of daminozide. Although the sample extracts were further cleaned by chromatography on silica gel, complex chromatograms were obtained. As can be seen in Figure 5, there are many eluting compounds with retention times near the elution of UDMH. These interfering compounds are less of a problem at concentrations of 1 ppm of daminozide/UDMH. However, they can prevent accurate detection and quantification of lower concentrations of daminozide/UDMH. Apple juice concentrate fortified with 0.1–5 ppm of daminozide and analyzed as UDMH-

bis(PFB) via GC–ECD showed recoveries of 65–95%, comparable with the results from the SIM–GC–MS analyses.

Figure 5 can be compared with mass chromatograms in Figures 3 and 4, respectively. The mass chromatogram at m/z 448 showed virtually no interferences. Some interference can be observed in the chromatograms for the lower mass ions (m/z 253 and others), but still those can be used for confirmational purposes or even increased detection with regard to an increased intensity of these ions.

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Registry No. UDMH, 57-14-7; SDMH, 540-73-8; UDMH-bis(PFB), 129918-74-7; SDMH-bis(PFB), 129918-75-8; daminozide, 1596-84-5; methylhydrazine, 60-34-4; hydrazine, 302-01-2; methylhydrazine-tris(PFB), 129918-76-9; hydrazine-tetrakis-(PFB), 129918-77-0.