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Technical note

Determination of 'common-batch' members in a set of confiscated 3,4-(methylendioxy)-methylamphetamine samples by measuring the natural isotope abundances: a preliminary study

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Abstract

$^{12}C/^{13}C$ natural isotopic abundances have been measured in a randomly chosen set of confiscated 3,4-(methylenedioxy)methylamphetamine (MDMA, XTC, Ecstacy) tablets using on-line gas chromatography isotope ratio mass spectrometry. The high precision obtained with this method allowed the discrimination of at least four different groups of MDMA tablets according to variations in their natural $^{13}C/^{12}C$ isotopic ratio. It is shown that further discrimination can be obtained by using the $^{15}N/^{14}N$ isotopic ratios in MDMA.

Keywords: Drugs analysis; Amphetamine; Designer drugs; 3,4-(Methylenedioxy)methylamphetamine; Natural isotopic abundances measurement; Discrimination of batches

1. Introduction

One of the ever returning questions in drug analysis concerns the origin of drug samples found at different locations at different times. The background to these questions is the hypothesis that there will be a fair possibility of linking together

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drugs stemming from the same production batch by chemical or physical methods. The evidential value of such links is well recognised, as this intelligence can be used to indicate how parts of a batch are spread over certain areas.

Usually the problem is tackled by (gas) chromatographic analysis of extracts of the drug samples in question, taking into consideration the impurities, found in minor quantities in the drugs, originating from improper purification of the drugs in the final stage of the production [1]. This so-called chemical signature analysis supported by computer processing and classification of the chromatographic results was applied successfully in the case of (Leuckart) amphetamine samples [2]. However, problems can arise in applying these techniques to amphetamines produced by methods in which relatively few impurities can be expected as in, for instance, the reductive amination route [3].

Nowadays the syntheses of the greater part of the 'designer drugs' have in common the use of essential oils as one of the starting chemicals [4,5]. No matter what kind of synthesis is used for the production of these drugs [3], the starting ketone is often prepared from natural products. The use of apiol, catechol, isosafrole, myristicinealdehyde, piperonal, safrole and sesamol for these purposes is mentioned in the literature [4].

Natural products have differing natural abundance ratios of $^{13}C/^{12}C$, $^{15}N/^{14}N$, $^{2}H/^{1}H$ and $^{18}O/^{16}O$ due to isotopic fractionation influenced by biochemical and environmental factors [6–8]. Accordingly, this gives us a further possibility to differentiate between batches of a drug produced from an essential oil as one of the starting compounds.

In this study $^{13}C/^{12}C$ and $^{15}N/^{14}N$ isotopic ratios are determined for a randomly chosen set of 3,4-(methylenedioxy)methylamphetamine (MDMA, XTC, Ecstacy). This was done in order to establish what kind of discrimination between the samples of the set could be reached by isotopic analysis.

2. Experimental

Randomly chosen tablets of MDMA from a collection of substances confiscated in the period 1989–1992 were investigated. They were undoubtedly synthesized from safrole or isosafrole as precursor (used as starting compound in the synthesis of piperonylmethylketone) [3]. For reference purposes pure MDMA was used.

2.1. Sample preparation for $^{13}C/^{12}C$ analysis [9]

A 50-mg quantity of a crushed MDMA tablet was taken up in 1 ml ammonium-nitrate. The solution was brought to pH 10 with ammonia. Then 1 ml of chloroform was added and the capped vial shaken on a Vortex for 1 min. After centrifugation and filtration a clear solution was obtained, of which an aliquot of 0.1–0.2 μl was injected into the GC-IRMS system.

2.2. Sample preparation for $^{15}N/^{14}N$ analysis

The same sample preparation method was used for $^{15}N/^{14}N$ analysis as in the $^{13}C/^{12}C$ analysis. However, 100 mg of a crushed tablet was taken and a dilute sodi-

um hydroxide solution was used in the extractions. After extraction of the aqueous alkaline solution with chloroform, centrifugation and filtration, the chloroform was evaporated under a mild stream of nitrogen. The residue was packed in a tin capsule and flash-burned at 1800°C. The gases were swept over a Cu-packed oven at 700°C using helium as carrier gas. In this way, nitrogen oxide gases were in-line reduced to nitrogen gas. Water, carbon dioxide and other trace gases were removed by using cryotraps and chemical traps, after which the nitrogen gas was introduced into a Finnigan MAT 251 gas isotope ratio mass spectrometer for $^{15}N/^{14}N$ analysis at *m/z* 28, 29, and 30. Calibration was against atmospheric nitrogen.

2.3. Gas chromatographic instrumentation

Gas chromatographic analysis of the $^{13}C/^{12}C$ chloroform extracts was done by using a Hewlett-Packard 5890 II gas chromatograph interfaced to a VG Isotech SIRA II isotope ratio mass spectrometer (model Isochrom I). A capillary column (25m × 0.25 mm i.d.) coated with a bonded OV-1 phase (0.25 μm film-thickness) was used. Helium was the carrier gas, the injection pressure was set at about 0.4 MPa and the injections were made in the splitless mode (injector temperature 250°C). The oven temperature was at 180°C. After chromatography, the GC effluent was sent either to the flame ionisation detector (FID) or to the isotope mass spectrometer via the combustion interface. In isotopic measurements the solvent peak was vented by means of switching a split valve. The combustion interface consisted of a quartz capillary furnace packed with copper oxide granules at 900°C. Organic compounds were combusted to carbon dioxide, water and trace gases. Water and trace gases were condensed using a capillary trap at −100°C, after which carbon dioxide was introduced into the mass spectrometer for $^{13}C/^{12}C$ analysis at *m/z* 44, 45 and 46. Results are expressed in the $\delta^{13}C$ notation (in permilles):

$$\delta^{13} = 10^{-3}[(^{13}C/^{12}C)_{sample} - (^{13}C/^{12}C)_{standard}]/ (^{13}C/^{12}C)_{standard}$$

Before and after the MDMA carbon dioxide peak, 30-s carbon dioxide reference gas pulses were introduced into the mass spectrometer for calculation of $\delta^{13}C$ values of the MDMA sample. The carbon dioxide reference gas is calibrated against NIST isotopic standards.

3. Results and discussion

3.1. Pure MDMA

A typical FID profile of a MDMA solution is shown in Fig. 1. No compounds other than MDMA could be detected by GC-FID. The precision and accuracy of the GC-IRMS method was tested by analysing a solution of the pure MDMA compound dissolved in methanol (see Table 1). For 0.1-μl injection volumes, the precision was found to be 0.21 permilles (n = 5). This value is slightly higher than values reported [10] for *n*-alkanes (0.008–0.17), but is better than the precision reported [11] for fatty acids (0.23–0.37). In Table 1 entries are given for different sample sizes and accuracy is found to be dependent on sample size. The $\delta^{13}C$ value of the pure

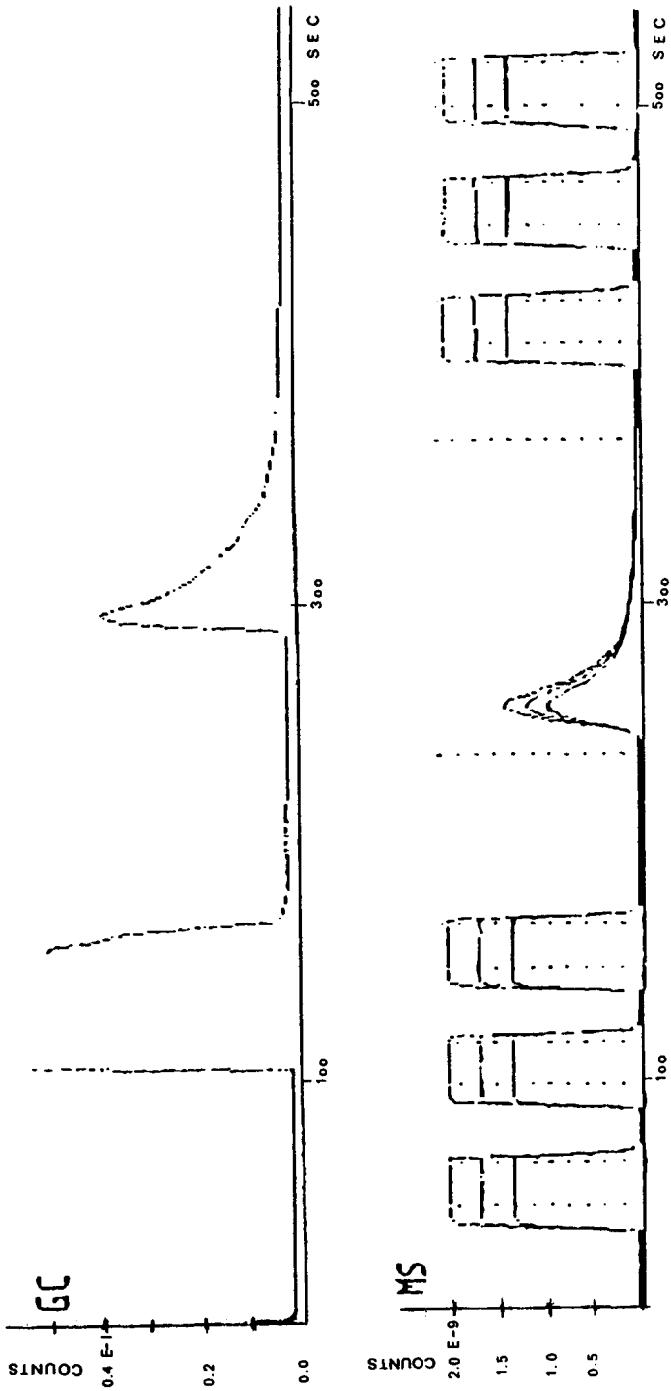

Fig. 1. GC-FID profile (top) and GC-IRMS trace (bottom). Flat topped peaks indicate reference gas pulses, sharp peaks represent MDMA.

Table 1
Accuracy and precision of $\delta^{13}C$ in pure MDMA measured by GC-IRMS

Injection volume (μl)	0.10	0.14	0.20
$\delta^{13}C$ (average)	−27.93	−28.17	−28.53
Number of injections	5	2	3
Standard deviation	0.21	n.d.	0.16

MDMA sample was also measured by on-line combustion isotope ratio mass spectrometry [12]. An average value of −28.00 permilles was obtained, in acceptable agreement with GC-IRMS results. These $\delta^{13}C$ are in the range of −24 to −34 permilles, typical for natural products from terrestial vegetation [13].

3.2. MDMA tablets

No other compounds were found by GC-FID analysis of the extracts of the tablets, with exception of samples 12 and 16 which were both found to contain additional amphetamine and caffeine. The $\delta^{13}C$ results of the GC-IRMS analyses on MDMA in tablets are shown in Table 2. Standard deviations obtained were in the range of 0.072–0.278 permilles, which were comparable with the variation of $\delta^{13}C$ in pure MDMA. Four groups of samples can be differentiated in view of the precision obtained (Fig. 2). One group consists of samples 5, 7, 13, and 14; the second

Table 2
$\delta^{13}C$ values and reproducibility of MDMA tablets

Sample	$\delta^{13}C$	S.D. (*n*)	R.S.D. (%)	$\delta^{15}N$
MDMA pure				
	−27.93	0.213 (5)	0.76	7.30
1	−27.82	0.184 (8)	0.66	−6.22
2	−27.27	0.140 (6)	0.51	−18.08
3	−28.21	0.210 (7)	0.74	
4	−27.16	0.181 (5)	0.67	
5	−29.35	0.184 (5)	0.63	
6	−27.32	0.131 (8)	0.48	
7	−29.36	0.277 (9)	0.94	
8	−27.26	0.247 (7)	0.91	2.96
9	−27.17	0.241 (5)	0.98	−16.15
10	−27.33	0.091 (4)	0.33	
11	−27.21	0.159 (7)	0.58	
12	−27.32	0.278 (4)	1.02	
13	−29.25	0.277 (9)	0.95	−16.35
14	−29.28	0.224 (7)	0.77	
15	−27.72	0.133 (7)	0.48	
16	−27.26	0.072 (4)	0.26	

Also shown are $\delta^{15}N$ values of some samples.

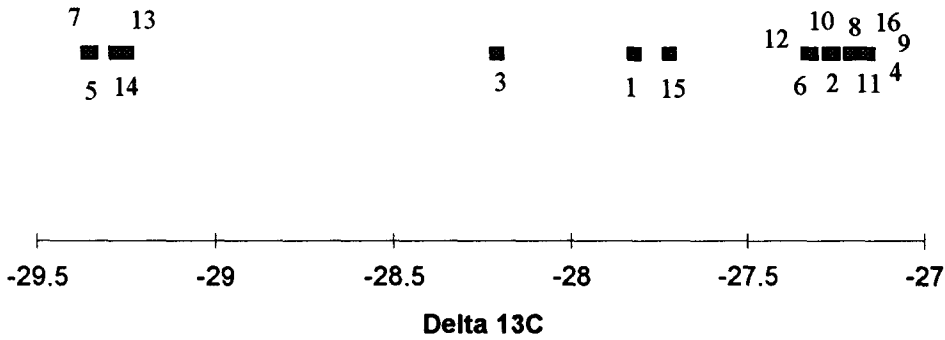

Fig. 2. $\delta^{13}C$ values for 16 samples of confiscated MDMA.

of sample 3, the third of samples 1 and 15 and the last and fourth of the rest (samples 2, 4, 6, 8–12, and 16).

In order of improve selectivity, the $\delta^{15}N$ of several samples were determined. Indeed, this additional parameter allowed further discrimination, it was now possible to show that samples 8 and 9 were different, although belonging to the same $\delta^{13}C$ group (Fig. 3).

4. Conclusions

On-line gas chromatography isotope ratio mass spectrometry (GC-IRMS) for the determination of natural $\delta^{13}C$ variations can be of help in discriminating sources of MDMA tablets. In this work four groups of MDMA were positively identified due to the satisfactory reproducibility of the $\delta^{13}C$ analyses. Further discrimination may be obtained by measuring $\delta^{15}N$ as an additional parameter. This case study also showed that $\delta^{13}C$ values were not conclusive: i.e., if the $\delta^{13}C$ values of drug samples were comparable, they may still originate from different batches. It would therefore be worthwhile in this type of study to increase the number of $\delta^{13}C$ values. This can in principle be obtained by chemical operations, in which the pure sample is converted c.q. degradated in different C-containing moieties, of which the $\delta^{13}C$ can then apart be measured by GC-IRMS [14].

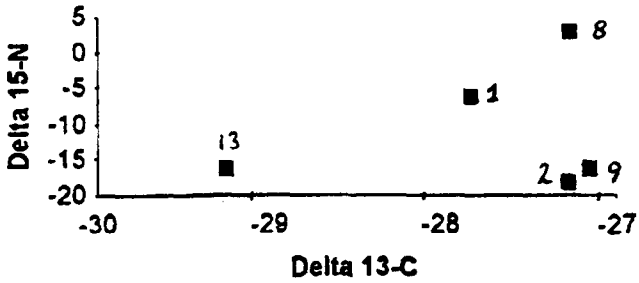

Fig. 3. Plot of $\delta^{15}N$ versus $\delta^{13}C$ for several MDMA samples.

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