Forensic Science International
94 (1998) 55–63

Detection of designer drugs in human hair by ion mobility spectrometry (IMS)

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Received 31 January 1997; received in revised form 20 May 1997; accepted 3 March 1998

Abstract

Since its inception in the early 1970s under the name plasma chromatography, ion mobility spectrometry (IMS) has undergone great changes. It is now utilized more and more in forensic science laboratories where it is used to detect explosives and environmental pollutants [1–4] as well as its use in detecting drugs of abuse [5–8]. Although IMS is known for nearly 30 years now [9], relatively few cases of the application of ion mobility spectrometry to the analysis of human hair have been reported [10–12]. The authors report a new and quick method to rapidly screen and determine MDMA (‘ecstasy’, ‘Adam’) and MDEA (‘Eve’) in human hair. The proposed method using trihexylamine as internal standard resulted in a rapid procedure useful in screening human hair specimens for designer drugs.

Keywords: Designer drugs; MDMA (‘Ecstasy’, ‘Adam’); MDEA (‘Eve’); Human hair; Ion mobility spectrometry; Internal standard

1. Introduction

Synthetic phenylalkylamine derivatives are known for their stimulant and/or hallucinogenic properties. 3,4-methylendioxymethamphetamine (MDMA), known as ‘ecstasy’ or ‘Adam’ and 3,4-methylendioxyethamphetamine (MDEA), are ring-substituted

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amphetamines that have appeared on the illicit market as 'designer' and 'rave' drugs produced in clandestine laboratories. First synthesized by Merck in 1914 and from 3,4-methylendioxyamphetamine (MDA), itself a drug of abuse (known as the 'love drug'), MDMA was originally developed as an appetite suppressant [13]. Also prescribed as an adjunct to psychotherapy [14], MDMA has emerged as a popular recreational drug over the last decade. It produces fewer of the visual, auditory and tactile hallucinations normally associated with psychedelics such as LSD [15]. MDEA, known as 'Eve', is a less toxic analog of MDMA with similar psychotropic effects in humans. Data on the pharmacology, pharmacokinetics and toxicology of designer drugs in humans are reviewed in the papers [16–32]. As a basis to documenting repeated or chronic drug abuse hair analysis was proposed. Unlike urine analysis, hair analysis provides the forensic chemist with long-term information of an individual's drug use. Previously reported methods for the determination of MDMA in human hair include GC/MS [33,34]. Not one paper mentions the detection of MDMA and MDEA by IMS. The purpose of this paper was to develop a method based on ion mobility spectrometry for the rapid screening of MDMA and MDEA deposited in human hair. Applying a simple sample pretreatment, the authors were able to detect these drugs semi-quantitatively within a short period of time. Confirmation analysis was performed by GC/MS.

2. Principle of IMS

Ion mobility spectrometry refers to the principles, practice and instrumentation for characterizing chemical substances through their gas-phase ion mobilities. IMS is an analytical technique that distinguishes ionic species on the basis of the differences in the drift velocity through a gas under an applied electrostatic field. It is a sensitive technique for the detection of trace organics under atmospheric pressure conditions. Fig. 1 depicts the schematic representation of the IONSCAN detection system. The sample, collected on a membrane filter for example, is heated to vaporization by the desorber. The neutral molecules of the vapor are carried in a stream of dried, filtered, ambient air through the heated transfer line into the reaction region. There, ionization is initiated by high energy electrons emitted from a ^{63}Ni beta-ray source. Every 20 ms the product ions (positive or negative) are gated with a pulse width of 0.02 ms into the heated drift region for mobility analysis. Under the influence of a controlled electric field and against a counterflow of ambient air drift gas the ions move to the collector electrode. The drift times needed by the ions to reach the collector electrode are proportional to their masses but inversely proportional to their characteristic reduced ion mobilities (K_0). For drug detection the ion mobility spectrometer is operated in the positive mode. In this mode the drift gas contains trace amounts of nicotinamide (NTA) used as both calibrant and reactant. In the reaction region the protonated nicotinamide transfers a proton to the sample molecule according to Eq. (1):

$$[\mathrm{NTA}]\mathrm{H}^+ + \mathrm{M} \rightarrow \mathrm{NTA} + [\mathrm{M}]\mathrm{H}^+ \quad (1)$$

This reaction only proceeds if the proton affinity of the sample molecule is greater then

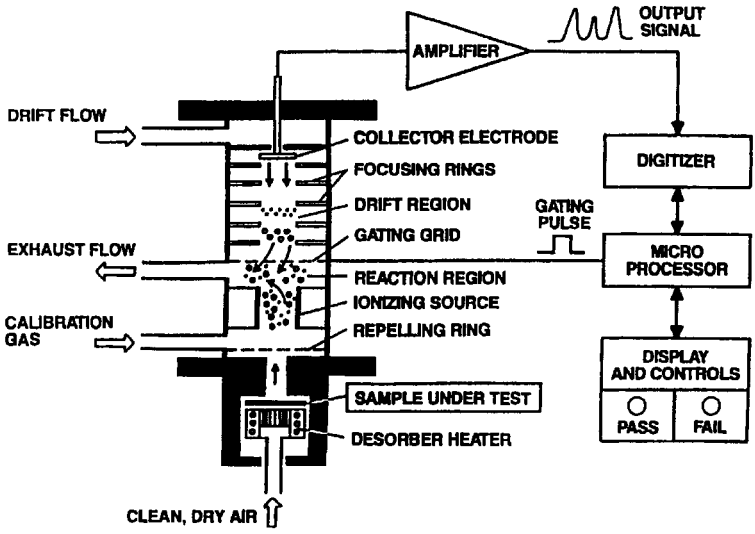

Fig. 1. Schematic representation of the IONSCAN 250 detection system.

that of nicotinamide. This is true for nearly all drug molecules which are thus detectable by IMS. The principles and theoretical background of ion mobility spectrometry has been extensively described elsewhere [35–39] and will not be discussed in this paper.

3. Hair analysis by IMS

3.1. Sample preparation

Human hair samples were obtained from the scalp of a drug addict. The powdered hair sample of an interlaboratory control for designer drugs in hair was also analyzed. Preparation of the hair samples was conducted according to Miki et al. [11]. In our approach trihexylamine (THA) was used as internal standard (I.S.). Prior to the measurements the specimens were thoroughly washed with 0.1% sodium dodecyl sulfate (SDS) solution. Then the samples were treated with distilled water and methanol by applying ultrasonification for 1 min (the washing process is necessary to remove any surface contaminations). After complete drying the hair specimens were pulverized using a ball mill. A 0.2-ml volume of 5 M methanolic sodium hydroxide solution (methanol/water 4:1) and 0.04 ml of the methanolic 1 ng μl^{-1} internal standard solution was added to 2 mg of the powdered, dry hair sample in a polyethylene tube. Ultrasonification of the samples was performed in a waterbath (45°C) and resulted in complete digestion of the samples within 20 min. Standards of known amounts of MDMA and MDEA were prepared by spiking blank hair samples to obtain final concentrations of 1, 2, 5, 10, 20 and 50 ng MDMA and MDEA/mg hair.

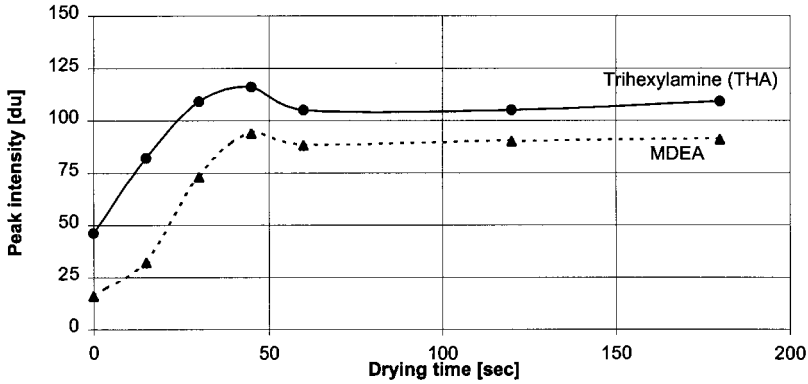

Fig. 2. Peak intensity versus drying time curve for MDEA and THA.

3.2. IMS measurement

An 0.05-ml aliquot of a digested hair sample solution was pipetted on a Teflon membrane filter in blots/splash. Under a gentle stream of warm air (from a hair dryer) the solvent was evaporated to dryness. Throughout the experiments a drying time of 45 s was applied. Fig. 2 shows the peak intensity versus drying time curves for MDEA and internal standard at the operated conditions (see Table 1). Fig. 3 represents the peak intensity versus desorber temperature curves for MDEA and trihexylamine, respectively. The calibration curve for MDMA and MDEA obtained by IMS assay of digested blank hair samples containing known amounts of drug is shown in Fig. 4.

Table 1
IONSCAN operation parameters

Parameter	Setting
Desorber temperature [°C]	240
Inlet temperature [°C]	287
Drift tube temperature [°C]	234
Drift flow [$cm^3\ min^{-1}$]	300
Sample flow [$cm^3\ min^{-1}$]	200
Exhaust flow [$cm^3\ min^{-1}$]	498
Drift gas	Dried air
Carrier gas	Dried air
Calibrant/reactant	Nicotinamide
Gate width [ms]	20
Scan cycle time [ms]	20
Drift tube length [cm]	7
Shutter grid pulse [μs]	200
Threshold [du]	2

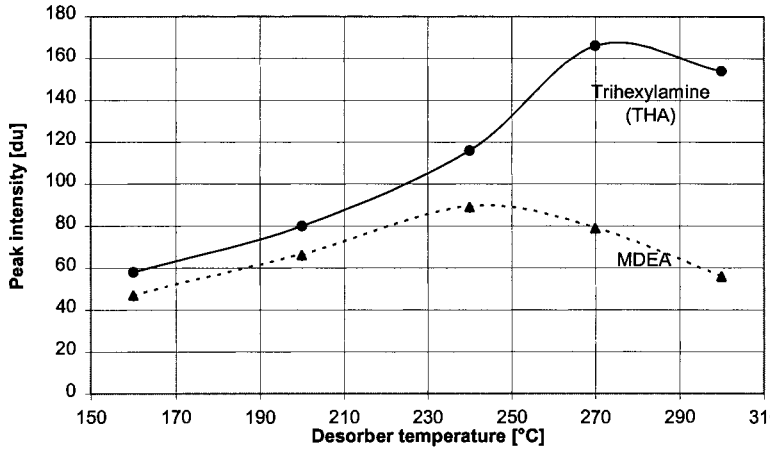

Fig. 3. Peak intensity versus desorber temperature curve for MDEA and THA.

4. Experimental

4.1. Chemicals and reagents

MDMA and MDEA methanolic standard solutions were obtained from Radian (Austin, TX, USA). Sodium hydroxide pellets, sodium dodecyl sulfate and methanol were of analytical grade and were obtained from E. Merck (Darmstadt, Germany). Trihexylamine was purchased from Aldrich-Chemie (Steinheim, Germany).

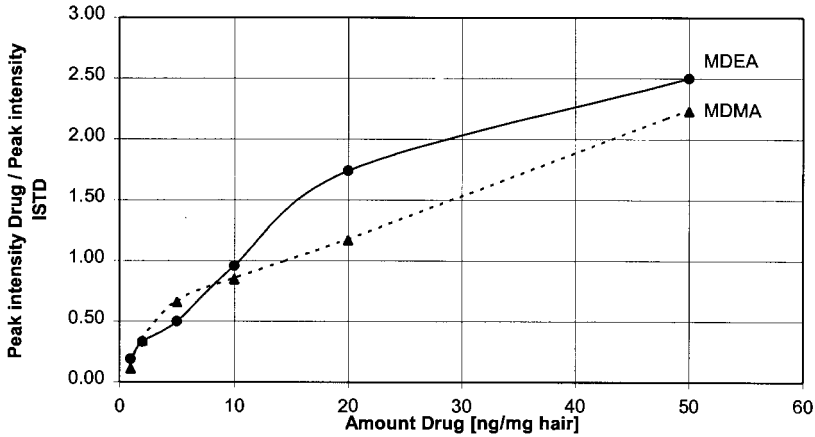

Fig. 4. Calibration curve for MDMA and MDEA.

4.2. Instrumentation

An IONSCAN Model 250 ion mobility spectrometer (Barringer, Rexdale, Canada) was used in the positive mode. Operation parameters are summarized in Table 1. Teflon membrane filters with a thickness of 0.25 mm were utilized as filter substrates.

5. Results

A typical plasmagram of a digested hair sample and internal standard (trihexylamine) is shown in Fig. 5. The peaks detected were identified as MDMA, MDEA and trihexylamine on both reduced ion mobility (K_0) and drift time (D_{Time}). Following IMS analysis of the hair samples, the ratio of the peak intensity (maximum peak amplitude) of MDMA and MDEA to that of the internal standard was determined for each digested hair sample. Semi-quantification of MDMA and MDEA present in the hair samples was achieved utilizing these experimental ratios, and a calibration curve constructed from the ratios obtained by IMS assay of blank hair samples containing known concentrations of MDMA, MDEA and the internal standard, trihexylamine. The corresponding calibration curve is depicted in Fig. 4. The relative standard deviation (R.S.D.) of MDEA and the internal standard (trihexylamine) at 10 ng mg^{-1} were 5.7% and 16.1%, respectively.

PK	Peak ID	Ko	DTime
0	Cal	1.8664	8.935
4	MDEA	1.4201	11.743
7	MDMA	1.4733	11.319
100	THA	1.0604	15.726

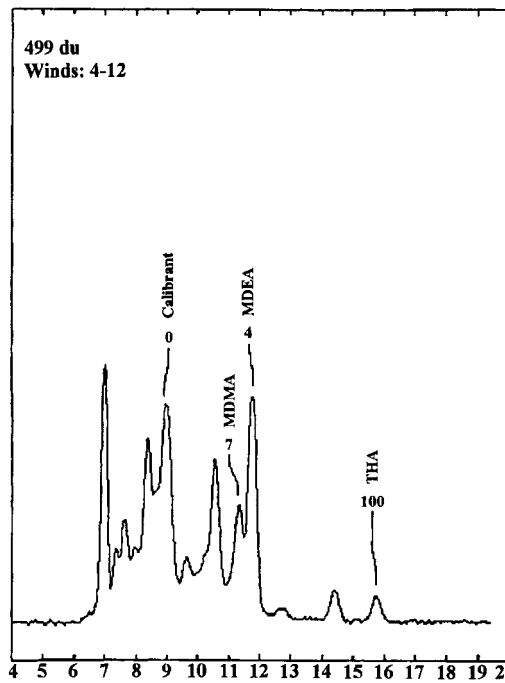

Fig. 5. Plasmagram of a digested hair sample (D_{Time} = 11.319 ms (MDMA); D_{Time} = 11.743 ms (MDEA); D_{Time} = 15.726 ms (ISTD, trihexylamine)).

Although the peaks for MDMA and MDEA are not clearly separated due to similar drift time, the ion mobility spectrometer could discriminate these two analogs. The internal standard, trihexylamine, was clearly separated from the designer drugs under consideration. Throughout the experiments the threshold was set at 2 du, the minimum value adjustable. The use of glass fiber filters resulted in poor plasmagrams due to too much background noise. Utilizing Teflon membrane filters was most effective for the analysis of hair samples digested under alkaline conditions. Fig. 3 shows the peak intensity versus desorber temperature curves for MDEA and the internal standard. A desorber temperature of 240°C resulted in a maximum peak intensity for MDEA. This desorber temperature was also chosen for the detection of MDMA. The corresponding peak intensity versus drying time curves for MDEA and trihexylamine are represented in Fig. 2. For both substances a drying time of 45 s resulted in a maximum peak intensity. Up to a drying time of 3 min the peak intensity recorded remained constant.

6. Discussion

By the use of the IMS technology the authors managed to establish a rapid, simple and sensitive screening method for the detection of the designer drugs MDMA and MDEA in human hair. To the best of our knowledge, no data is available on MDMA and MDEA testing in human hair by ion mobility spectrometry. The only drugs on which hair analysis by IMS has recently been reported are cocaine, clenbuterol and methamphetamine [10,11]. Moreover, Miki et al. [11] were the first ones to use an internal standard for IMS measurements. As far as we are aware there are only a few papers that deal with the analysis of MDMA in human hair [33,34]. In the cited papers, hair analysis was performed by GC/MS. Kintz et al. [33] had also used a sodium hydroxide solution to destroy the protein matrix of the hair. They had incubated 30 mg hair in 1 ml 1 M sodium hydroxide for 10 min at 95°C. In our approach the use of 0.02 ml 5 M NaOH solution resulted in complete digestion of 2 mg hair after 20 min. Digestion was achieved by ultrasonification in a waterbath at 45°C. The presented study indicated that IMS can be a simple and rapid tool for the detection of MDMA and MDEA in human hair. The advantages of ion mobility spectrometry are not only the very short analysis time (5–8 s), its detection limits in the nanogram to picogram range but also the possibility to analyze solid and pulverized specimens as well as samples in solution. According to the authors' opinion, additional studies on a wider range of drugs are needed to further investigate the applicability of ion mobility spectrometry to cases of clinical and forensic relevance [8,39].

Acknowledgements

The authors gratefully thank Juergen Baller for his critical review of the manuscript and Wolfgang Meyer for his excellent and skilfull technical assistance.

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