Journal of Chromatography, 580 (1992) 125–134
Biomedical Applications
Elsevier Science Publishers B.V., Amsterdam

CHROMBIO. 6355

Review

Drug detection in hair by chromatographic procedures

Manfred R. Moeller

Institut für Rechtsmedizin der Universität des Saarlandes, W-6650 Homburg/Saar (Germany)

(First received January 28th, 1992; revised manuscript received April 29th, 1992)

ABSTRACT

This article reviews the analysis of 31 drugs and drug metabolites in human hair by thin-layer chromatography, high-performance liquid chromatography, gas chromatography, gas chromatography–mass spectrometry and mass spectrometry. The most important detection method after chromatographic separation of the components is the mass spectrometry because of its sensitivity and specifity. Washing steps to exclude external contamination, extraction, derivatization, stationary phases, detection modes and detection limits of the mass spectrometric and gas chromatographic–mass spectrometric procedures are presented in five tables. Additionally, a method for a gas chromatographic–mass spectrometric screening procedure is presented.

CONTENTS

Correspondence to: Dr. M. R. Moeller, Institut für Rechtsmedizin der Universität des Saarlandes, W-6650 Homburg/Saar, Germany.

0378-4347/92/$15.00

LIST OF ABBREVIATIONS

AA	Acetic anhydride
AC	Acetone
AL	Alkaline-hydrolysed
BP	Benzophenone
BSTFA	N,O-Bis(trimethylsilyl)trifluoroacetamide
CC	Capillary column
CI	Chemical ionization
CS	Collisional spectroscopy
DECON	Removal of external contamination
DER	Derivatizing reagent
DET	Detergent
DETMODE	Detection mode
DIP	Direct insertion probe
D.I.S.	Deuterated internal standard
EI	Electron-impact ionization
EN	Enzymic cleavage of conjugates
E.S.	External standard
ET	Ether
EX	Liquid–liquid extraction
FID	Flame ionization detection
GC	Gas chromatography
GC–MS	Gas chromatography mass spectrometry
HFBA	Hexafluorobutyric acid
HPLC	High-performance liquid chromatography
HPTLC	High-performance thin-layer chromatography
HY	Acid-hydrolysed
I.S.	Internal standard
MBTFA	N-Methylbistrifluoroacetamide
ME	Methylated/methylation
MeOH	Methanol
MS	Mass spectrometry
MTBSTFA	N-Methyl-N-(*tert.*-butyldimethylsilyl)trifluoroacetamide
m/z	Mass-to-charge ratio
NP-FID	Nitrogen–phosphorus flame ionization detection
PC	Packed column
PFB	Pentafluorobenzyl bromide
PFPA	Pentafluoropropionic anhydride
PFPOH	Pentafluoropropionyl alcohol
QUANT	Quantitation
RIA	Radioimmunoassay
SDS	Sodium dodecyl sulphate
SIM	Selected-ion monitoring
SP	Solid-phase extraction
TBA	Tetrabutylammonium hydrogensulphate
TFAA	Trifluoroacetic anhydride
THC	Δ^9-Tetrahydrocannabinol
THC-COOH	11-Nor-9-carboxy-Δ^9-tetrahydrocannabinol
TLC	Thin-layer chromatography

1. INTRODUCTION

Casper [1] reported in 1857 the analysis of hair for the detection of poisons in his famous *Praktisches Handbuch der gerichtlichen Medizin*. He referred to Hoppe-Seyler, who had found arsenic in the hair of a body buried for 11 years and had discussed the possibility that the metal was incorporated before death. About one hundred years later, the first report of the detection of an organic drug in hair was published. Goldblum *et al.* [2] described in 1954 an ultraviolet method to detect barbiturates in guinea-pig hair.

Baumgartner *et al.* [3] published a radioimmunological (RIA) method for the detection of opiates in the hair of addicts. The proof of morphine in head hair by thin-layer chromatography (TLC) was reported by Klug [4]. Suzuki *et al.* published a method for the detection of methamphetamine and amphetamine in a single human hair by mass spectrometry (MS) [5,6]. The detection of morphine in hair by high-performance liquid chromatographic (HPLC) was reported by Marigo *et al.* [7].

Meanwhile, the aim of more detailed investigations is the quantitation of the drugs and drug metabolites in hair.

This review concentrates on chromatographic techniques because they are the most powerful tools for the identification and quantitation of drugs in hair, owing to their separation ability and their detection sensitivity. TLC and HPLC methods are presented first, followed by gas chromatographic (GC) and gas chromatograph-

ic–mass spectrometric (GC–MS) procedures for individual drugs and drug metabolites. Finally, a method for GC–MS screening for drugs and drug metabolites in hair is presented.

2. ANALYTICAL PROCEDURES FOR THE DETECTION OF DRUGS IN HAIR

2.1. Non-chromatographic methods

In 1979 Baumgartner *et al.* [3] published a method for "radioimmunoassay of hair for determining opiate-abuse histories". This first publication was followed by a number of papers, which included the radioimmunological detection of phenobarbital [8], cocaine and benzoylecgonine [9,10], methadone [11], Δ^9-tetrahydrocannabinol carboxylic acid (THC-COOH) [12,13], haloperidol [14], phencyclidine [15], digoxin [13] and miscellaneous others [16]. Other immunological techniques [17,18] were also used. However, the specificity of most immunoassays is directed to a group of drugs and drug metabolites rather than to a single substance. So quantitation by immunoassay is not possible [19]. Additionally, positive results of urine analysis must be confirmed by a more specific method, preferably by GC–MS.

2.2. Chromatographic procedures for individual drugs and drug metabolites

2.2.1. Thin-layer chromatography

In 1980 Klug [4] reported a TLC method to detect morphine in the head hair of drug abusers. He dissolved the hair in sodium hydroxide and hydrolysed the solution with hydrochloric acid. He extracted the solution with amyl alcohol and separated the components by TLC. Detection and quantitation were made by fluorimetry. The findings were between traces and 4 ng/mg. A high-performance thin-layer chromatographic (HPTLC) method was used to determine morphine in human hair [20]: 20–200 mg of hair were washed four times with water to remove surface contamination. Then the hair was incubated in sodium hydroxide and subsequently in hydrochloric acid at 80°C in both cases. After solid phase extraction on Extrelut 3 (Merck) the solution was dansylated, analysed by HPTLC (methanol–ammonia, 99:1) and quantitated by densitometry.

2.2.2. High-performance liquid chromatography

An HPLC method to detect morphine in hair samples was reported by Marigo *et al.* [7]. They tested several washing and dissolving procedures for the hair and decided to use a single acid washing with dilute hydrochloric acid. After incubation of the hair sample with dilute hydrochloric acid they performed a solid-phase extraction and dansylated the extract. They used silica as a stationary phase with hexane–2-propanol–ammonia (95:4.5:0.5, v/v/v) as mobile phase and fluorescence detection to identify and quantitate the morphine. They found a good correlation of the amounts detected in the hair of heroin addicts by HPLC and by RIA ($r = 0.997$; $n = 15$).

The separation of the optical isomers of methamphetamine and amphetamine from hair by HPLC was reported [21,22]. A rather large amount of hair (200–250 mg) from stimulant abusers was used as specimen. After acetylation the samples were chromatographed on a column that contained an optical active carrier (Chiracel OB) and *n*-hexane–2-propanol as mobile phase to separate the *d*- and *l*-isomers of methamphetamine and amphetamine. Only *d*-methamphetamine and *d*-amphetamine could be found in the hair of the abusers.

Haloperidol and its major active metabolite, reduced haloperidol, were detected in hair samples by isocratic HPLC [14]. The hair samples were dissolved by different methods (sonicated in 0.1% SDS solution or methanol or in 2 *M* NaOH at 80°C). Dissolution in NaOH gave the best results. The samples were chromatographed on a TSK Gel-TM ODS column with potassium phosphate buffer–acetonitrile–methanol (3:2:1, v/v/v) as the mobile phase and detected coulometrically. The concentration of haloperidol was determined by RIA in parallel. Values showed good correlation. The concentrations of haloperidol and reduced haloperidol measured in hair correlated

better than those measured in serum with the individual dosage history.

2.2.3. Gas chromatography

GC procedures are less useful for the analysis of drugs in hair. The enormous number of possible exogenous and endogenous compounds that can be found in hair makes the interpretation of chromatograms with flame ionization detection (FID) or even nitrogen–phosphorus flame ionization detection (NP-FID) very difficult. The number of papers is thus very limited.

Viala *et al.* [46] published a GC method for chloroquine and monodesmethylchloroquine in the hair of patients who had been treated with chloroquine for several months. The samples were washed with detergent and then dissolved in hot potassium hydroxide. After the extraction with diethyl ether a thin-layer procedure was used for cleaning up. The quantitation was made by GC–NP-FID. Chloroquine and its metabolite were identified by GC–MS. The GC analysis of chloroquine with NP-FID was reported by Ochsendorf *et al.* [26]. They quantitated the drug in different hair sections and found a correlation with the pharmacological behaviour of the substance.

Takahashi [23] reported the detection of methamphetamine and amphetamine in hairs of monkeys after administration of methamphetamine. He used trifluoroacetic anhydride (TFAA) for derivatization and a GC column packed with OV-101. He found the highest amount of both compounds in the fourth week, then they decreased gradually. Nagai *et al.* [24] presented a method for the detection of methamphetamine and amphetamine in the hair of addicts, as well as in hair, bones and teeth after animal experiments. They used a packed column with 5% PEG 6000 with 5% KOH and N-ethylbenzylamine as the internal standard.

Ishiyama *et al.* [25] found amitriptyline, imipramine and their metabolites in the hair of patients on long-term treatment with antidepressants. They also found methamphetamine and amphetamine in the hair of addicts, and nicotine in the hair of smokers. To detect the amphetamines, the hair was dissolved by treating with NaOH and then HCl, extracted with chloroform, trifluoroacetylated and analysed on an OV-17

TABLE I

GC–MS ANALYSIS FOR INDIVIDUAL DRUGS AND DRUG METABOLITES IN HAIR

Drug/metabolite	Decontam.	Work-up	Derivative	GC column	DetMode	Quant.	Det.limit	Ref.
Methamphetamine	DET–HCl	HY-EX	TFA	OV-17 PC	EI-SIM		0.1 ng	27
Methamphetamine	MeOH–H_2O	AL-EX	TFA	OV-17 PC	EI-SIM	I.S.		25
Methamphetamine amphetamine		AL-EX	TFA	Thermon PC-3000	CI-SCAN EI-SCAN	I.S.	0.01 ng	6
Methamphetamine, amphetamine	–	AL-EX	TFA	Thermon PC-3000	CI-SCAN EI-SCAN	I.S.	0.01 ng	5
Methamphetamine	HCl–MeOH	HY-EX	TFA	OV-17 PC	EI-SIM		1 ng	29
Methamphetamine, amphetamine	MeOH–H_2O	HY-EX	TFA	–		–	0.02 ng 0.1 ng	28
Methamphetamine, amphetamine	–	AL-EX	TFA	OV-17 PC	EI-SCAN	–		24
Methamphetamine, amphetamine, *p*-OH-methamphetamine	MeOH–H_2O	HY-EX	TFA	OV-17 PC	EI-SIM	E.S.	0.02 ng 0.02 ng 0.1 ng	47
Methamphetamine, ampethamine	SDS–H_2O	HY-EX	TFA	WCOTCC	EI-SIM	D.I.S.	0.5 ng/mg	48

column. The antidepressants were extracted with heptane and analysed on an OV-17 column.

GC detection of chartering with NP-FID was reported by Ochsendorf *et al.* [26]. They quantitated the chartering in different hair sections and found a correlation with the pharmacognosy of the substance.

2.2.4. Gas chromatography–mass spectrometry

GC–MS is the most powerful tool for the detection of drugs in hair. The most important conditions of the investigations are presented in Tables 1–5, ordered by substance groups. Listed are the method of removal of external contamination (Decontam.), the work-up procedure, containing a possible acid (HY), alkaline (AL) or enzymic (EN) hydrolysis and the method of extraction: solid phase (SP) or liquid–liquid extraction, conditions of derivatization, the instrument requirements *e.g.* gas chromatographic column, detection mode (DetMode), the type of quantitation (with internal standard (I.S.), deuterated internal standard (D.I.S.) or external standard (E.S.)) and the detection (Det.) limits.

2.2.4.1. Amphetamines. Eight GC–MS procedures (Table 1) for methamphetamine were described. The papers published in Japanese [5,21,27,28] have corresponding abstracts in English [6,22,29,30]. Methamphetamine was detected and determined by MS in rat hair after administration of the substance [27]. Six methods also detected the metabolite amphetamine. Suzuki *et al.* [47] determined methamphetamine in nails, sweat and saliva. The work-up (liquid–liquid extraction after acid or alkaline hydrolysis) and derivatization techniques (TFA) are similar in all procedures.

2.2.4.2. Cannabinoids. The detection of cannabinoids in hair by GC–MS seems to be more difficult, because there are only three reports (Table 2) in the literature. Balabanova *et al.* [12] published a method with RIA detection of cannabinoids and GC–MS confirmation of Δ^9-THC. However, the SIM chromatograms shown in the publication are very poor [31,32]. For the detection of THC-COOH [33] the hair was hydrolysed in alkaline solution, extracted on Baker C_{18} columns from acid solution, and derivatized with methyl iodide. THC-COOH was quantified after similar work-up and extraction, and derivatization with pentafluoropropionic anhydride (PFPA) and pentafluoropropionyl alcohol (PFPOH), with levallorphan as I.S. [34].

2.2.4.3. Cocaine and metabolites. Procedures for the detection of cocaine and/or its metabolites have been published in ten papers (Table 3). There is considerable variety in the work-up and derivatization conditions. Decontamination seems to be a problem, because cocaine could not be washed out from hair soaked with the drug [35], so a passive contamination cannot be excluded. The determination of the metabolites may help to solve the problem [35,36]. It seems that the substances are incorporated according to their lipophilicity, because cocaine is found in most cases in the higher concentrations than benzoylecgonine and methylecgonine [35,37,38]. Some papers describe detection by MS or MS–MS after direct inlet of the probe [37,39,40]. Because of their scientific relevance and the fact that

TABLE 2

GC–MS ANALYSIS FOR INDIVIDUAL DRUGS AND DRUG METABOLITES IN HAIR

Drug/metabolite	Decontam.	Work-up	Derivative	GC column	DetMode	Quant.	Ref.
Δ^9-THC	–	HY	–	DB-1	EI-SIM	–	12
THC-COOH	H_2O AC	AL-SP	MET	HP-1	EI-SIM	–	33
THC-COOH	H_2O–AC	AL-SP	PFPA–PFPOH	HP-1	EI-SIM	I.S.	34

TABLE 3

GC–MS ANALYSIS FOR INDIVIDUAL DRUGS AND DRUG METABOLITES IN HAIR

Drug/metabolite	Decontam.	Work-up	Derivative	GC column	DetMode	Quant.	Det.limit	Ref.
Cocaine	H_2O-EtOH	HY-EX	–	OV-1-CC	EI-SIM	–	–	49
Benzoylecgonine	Soap-AC	HY-EX	PFB–TBA	ISOT-CC	EI-SIM	E.S.	0.05 ng	50
Cocaine, benzoylecgonine	MeOH	SP	–	–	CI-MS–MS	D.I.S.	–	39
Cocaine, benzoylecgonine	MeOH	SP	–	–	EI-SCAN	D.I.S.		39
Cocaine, benzoylecgonine, ecgonine	–				CI-MS–MS	E.S.	–	37
Benzoylecgonine	H_2O–AC	EX	BSTFA	DB-5 CC	EI-SIM	D.I.S.		51
Cocaine, benzoylecgonine methylecgonine	H_2O–AC	EN-SP	PFPA–PFPOH	HP-2 CC	EI-SIM	D.I.S.	0.1 ng/mg	38
Cocaine, benzoylecgonine, methylecgonine	SDS MeOH	EN-SP	MTBSTFA	DB-5 CC	CI-SIM	I.S.	0.1 ng/mg	36
Cocaine, cocaethylene, norcocaine	MeOH at 37°C	HY-SP	BSTFA	HP-1 CC	EI-SIM	D.I.S.	0.1 ng/mg	351
Cocaine, benzoylecgonine	MeOH	HY-SP	–	–	CI-MS–MS	D.I.S.	–	40

TABLE 4

GC–MS ANALYSIS FOR INDIVIDUAL DRUGS AND DRUG METABOLITES IN HAIR

Drug/metabolite	Decontam.	Work-up	Derivative	GC column	DetMode	Quant.	Det.limit	Ref.
Codeine	–	–	–	OV-17 PC		–	–	41
Morphine, codeine	Soap–AC	HY-EX	HFBA	Ultra 2 CC	EI-SIM	I.S.	–	52
Morphine	ET–HCl	HY-SP	–	–	EI-CS	–	1–10 fg	42
Morphine	CH_2Cl_2	AL-EX	AC	OV-1 CC	EI-SIM		0.05 ng/mg	53
Morphine, codeine, dihydromorphine, dihydrocodeine	AC	HY-SP	HFBA	Ultra 2 CC	EI-SIM	I.S.	–	33
Morphine, codeine	MeOH	AL-SP	PFPA	HP-1 CC	EI-SIM	I.S.	5 ng	54
Pholcodine	AC	HY-SP	AA	HP-1 CC	EI-SCAN	–	0.3 ng/g	55
Dihydrocodeine	AC	AL-SP	HFBA	Ultra-2 CC	EI-SIM	I.S.	0.03 ng	56
Heroin, 6-acetylmorphine, morphine, codeine	MeOH at 37°C	EX	MBTFA	HP-5 CC	EI-SIM	D.I.S.	0.1 ng/inj.	43
6-Acetylmorphine, morphine, codeine	MeOH–AC	EN-SP	HFBA	Ultra-2 CC	EI-SCAN	I.S.	–	59

a similar detection technique is used, they are included in this review. There are several advantages of direct insertion probe (DIP) and chemical ionization mass spectrometry (CI-MS–MS) over electron-impact ionization with selected-ion monitoring (EI-SIM) [37], although the preferred routine method for the quantitation is GC–MS [39].

2.2.4.4. Opiates. Ten papers deal with the GC–MS detection of six different opiates in hair (Table 4). The first report, published in 1984 [41] dealt with codeine detection in animal hair after administration of the drug. Again one paper describes direct insertion of the probe and chemical ionization [42]. As heroin samples always contain codeine as an impurity, this substance also can be detected in cases of heroin abuse. Morphine is a metabolite of codeine and can be detected when codeine is abused. The quantitation of both drugs allows differentiation between codeine and heroin abuse [33]. The detection of 6-acetylmorphine raises the possiblity of proving directly the abuse of heroin [43]. Here also the more lipophilic 6-acetylmorphine exceeds the morphine in most samples.

2.2.4.5. Miscellaneous. Table 5 lists those drugs that have been detected in hair, but do not belong to one of the groups above. Ishiyama *et al.* [25] detected tricyclic antidepressants in hair and discussed the possibility of definite determination if patients are under long-term treatment of medicines. Pentazocine was abused by a medical doctor and could be detected by hair analysis [44]. In patients under methadone treatment, hair analysis perhaps may show a dose related concentration.

2.3. Chromatographic screening procedures

The simultaneous analysis of hair for several drugs of abuse was demonstrated by Moeller and Fey [34]. The hair was washed with warm water and acetone, pulverized, incubated with diluted NaOH, extracted on a solid phase and derivatized with PFPA–PFPOH. The chromatography was carried out on an HP-1 capillary column. The different substances (amphetamine, morphine, codeine and THC-COOH) were analysed in one run using the EI-SIM technique. For each compound two m/z values were used.

Amphetamine, cocaine, benzoylecgonine, codeine, morphine and THC-COOH [58] were ana-

TABLE 5

GC–MS ANALYSIS FOR INDIVIDUAL DRUGS AND DRUG METABOLITES IN HAIR

Drug/metabolite	Decontam.	Work-up	Derivative	GC column	DetMode	Quant.	Det.limit	Ref.
Amitriptyline, nortriptyline	DET–SDS	AL-EX	–	OV-17 PC	EI-SIM	I.S.	–	25
Imipramine, demethylimipramine	DET SDS	AL-EX	–	OV-17 PC	EI-SIM	I.S.	–	25
Nicotine	DET–SDS	AL-EX		OV-17 PC	EI-SIM	I.S.	–	25
Chloroquine, monodesmethyl-chloroquine	DET–H_2O	AL-EX	–	OV-1 CC	NCI	–	–	46
Methadone	–	HY-EX	–	DB-1 CC	EI-SIM	–	6 pg/inj.	57
Phencyclidine	–	–	–	–	CI-MS–MS			37
Bromazepam	H_2O–AC	HY-SP	BP	HP-1 CC	NCI-SCAN	I.S.	–	58
Oxazepam	H_2O–AC	HY-SP	BP	HP-1 CC	EI-SIM	I.S.	–	58
Nicotine	H_2O–AC	HY-SP	–	HP-1 CC	EI-SIM	–		58
Caffeine	H_2O–AC	HY-SP	–	HP-1 CC	EI-SIM	–	–	58
Pentazocine	H_2O–AC	EN-AL-SP	PFPA–PFPOH	HP-1 CC	EI-SIM	I.S.	–	44

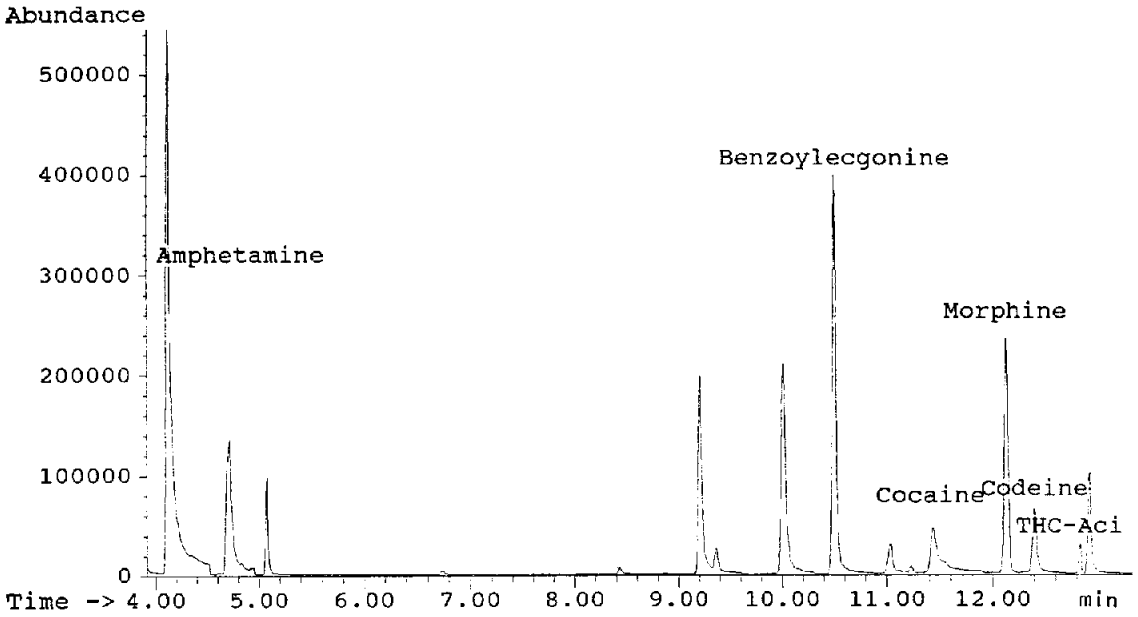

Fig. 1. Total ion chromatogram of a hair extract, spiked with a mixture of deuterated standards (10 ng per injection) of amphetamine, benzoylecgonine, cocaine, codeine, morphine and THC-COOH [44]. Details of the method are described in Section 2.3, retention times in min.

lysed from hair samples in one procedure. The hair was washed with warm water and acetone. After pulverization and addition of the I.S. levallorphan, the hair was treated with 2% NaOH for 30 min. After addition of 3 ml of 2% HCl, the solution was incubated overnight at room temperature. The solution was separated and the residue of the hair dissolved in NaOH. Both solutions were buffered to pH 8, extracted on a solid phase (Bakerbond^{R} Octadecyl) with dichloromethane–acetone, derivatized with PFPA–PFPOH, and analysed by GC–MS using the EI-SIM technique. In an improved procedure, the deuterated analogues of the drugs were used and the hair was preincubated with glucuronidase–arylsulphatase (Fig. 1) [44].

3. CONCLUSIONS

The concentrations of drugs in hair are in the ng/mg range, at least in cases of chronic abuse. No information is available about the minimum dose of drug intake, which can be detected by hair analysis. Calculation by Sachs and Moeller [60] assume that for heroin, one or two injections per week lead to a concentration of morphine of 0.5–1 ng/mg hair. This is the detection limit of the routine GC–MS methods described. Depending on the amount of specimen used, immunoassays are a good method of preanalysing hair samples. In positive cases, the results must be confirmed by a more specific method. Here the GC–MS procedure is state of the art. That is clearly shown by this review: the GC–MS methods exceed by far all other chromatographic methods used.

The meaningfulness of hair analysis for drugs is a different time frame and quality of results, compared with blood and urine analysis. Hair analysis cannot show very recent drug use: because hair grows at 1–1.2 cm/month, there is a delay of several days between drug incorporation into the hair root and appearance of that hair section on the surface of the skin. Additionally, a single drug use cannot be detected with routine procedures but, by sectional analysis, the history of frequent or chronic drug use can be traced back for months, depending on the length of the hair. However, positive results are controversial [45]. The question of whether the drugs are at least partly incorporated by external contamina-

tion, and whether this external contamination can be totally washed out, is still unanswered.

Independent of this controversy, hair analysis for drugs offers a way to uncover chronic use in cases where blood or urine analysis fails [44]. The detection of the parent drug and the metabolites seems to be a way of deciding whether the drug has been incorporated or not. In cases of incorporation the concentration of the more lipophilic parent drug nearly always seems to be higher than that of the metabolite [37–39,43,59], in contrast to what happens in urine samples.

4. ACKNOWLEDGEMENTS

I thank Peter Fey for his assistance in preparing this review, and Thomas Krämer for Online research in the Medline database.

REFERENCES

1 J. L. Casper, *Praktisches Handbuch der gerichtlichen Medizin*, (2 vols.), A. Hirschwald, Berlin, 1857–1858.
2 R. W. Goldblum, R. L. Goldbaum and W. N. Piper, *J. Invest. Dermatol.*, 22 (1954) 121.
3 A. M. Baumgartner, P. F. Jones, W. A. Baumgartner and C. T. Black, *J. Nucl. Med.*, 20 (1979) 748.
4 E. Klug, *Z. Rechtsmed.*, 84 (1980) 189.
5 O. Suzuki and H. Hattori, *Koenshu-Iyo Masu Kenkyukai*, 8 (1983) 201.
6 O. Suzuki, H. Hattori and M. Asano, *J. Forensic Sci.*, 29 (1984) 611.
7 M. Marigo, F. Tagliaro, C. Poiesi, S. Lafisca and C. Neri, *J. Anal. Toxicol.*, 10 (1986) 158.
8 F. P. Smith and D. A. Pomposini, *J. Forensic Sci.*, 26 (1981) 582.
9 A. Valente, M. Cassini, M. Pigliapochi and G. Vansetti, *Clin. Chem.*, 27 (1981) 1952.
10 W. A. Baumgartner, C. T. Black, P. F. Jones and W. H. Blahd, *J. Nucl. Med.*, 23 (1982) 790.
11 S. Balabanova and H. U. Wolf, *Z. Rechtsmed.*, 102 (1989) 1.
12 S. Balabanova, P. J. Arnold, V. Luckow, H. Brunner and H. E. Wolf, *Z. Rechtsmed.*, 102 (1989) 503.
13 W. A. Baumgartner, V. A. Hill and W. H. Blahd, *J. Forensic Sci.*, 34 (1989) 1433.
14 H. Matsuno, T. Uematsu and M. Nakashima, *Br. J. Clin. Pharmacol.*, 29 (1990) 187.
15 A. M. Baumgartner, P. F. Jones and C. T. Black, *J. Forensic Sci.*, 26 (1981) 576.
16 W. Arnold, *J. Clin. Chem. Clin. Biochem.*, 25 (1987) 753.
17 A. Franchesin, L. Morosini and L. Dell'Ana, *Clin. Chem.*, 33 (1987) 2125.
18 Y. Yamamoto and K. Yamamoto, *Nippon Hoigaku Zasshi*, 34 (1980) 158.
19 R. C. Baselt, *J. Anal. Toxicol.*, 13 (1989) 1.
20 A. N. Jeger, R. E. Raas, C. Hamberg and Th. Briellmann, *Camag Bibliography Service*, 68 (1992) 7.
21 T. Nagai, M. Takahashi, K. Saito, S. Kamiyama and T. Nagai, *Igaku to Seibutsugaku*, 115 (1987) 147.
22 T. Nagai, S. Kamiyama and T. Nagai, *Z. Rechtsmed.*, 101 (1988) 151.
23 K. Takahashi, *Nippon Hoigaku Zasshi*, 38 (1984) 319.
24 T. Nagai, T. Nagai and T. Ikeda, in N. Dunnett and K. J. Kimber (Editors), *TIAFT Proceedings of the 21th International Meeting, Brighton*, McMillan, New York, 1984, p. 89.
25 I. Ishiyama, T. Nagai and S. Toshida, *J. Forensic Sci.*, 28 (1983) 380.
26 F. R. Ochsendorf, H. Schöfer, U. Runne, K. Schmidt and H. W. Raudonat, *Z. Rechtsmed.*, 31 (1989) 866.
27 S. Suzuki, T. Inoue and T. Niwaguchi, *Koenshu-Iyo Masu Kenkyukai*, 6 (1981) 129.
28 S. Suzuki, T. Inoue, T. Yasuda, T. Niwaguchi, H. Hori and S. Inayama, *Eisei Kagaku*, 30 (1984) 23.
29 T. Niwaguchi, S. Suzuki and T. Inoue, *Arch. Toxicol.*, 52 (1983) 157.
30 S. Suzuki, T. Inoue and T. Yasuda, in N. Dunnett and K. J. Kimber (Editors), *TIAFT Proceedings of the 21th International Meeting, Brighton*, McMillan, New York, 1984, p. 95.
31 H. Käferstein and G. Sticht, *Z. Rechtsmed.*, 103 (1990) 393.
32 M. Bogusz, *Z. Rechtsmed.*, 103 (1990) 621.
33 H. Sachs and M. R. Moeller, *Fresenius Z. Anal. Chem.*, 334 (1989) 713.
34 M. R. Moeller and P. Fey, *Bull. Soc. Sci. Med. Grand Duché Luxembourg*, 127 Suppl. (1990) 460.
35 E. J. Cone, D. Yousefnejad, W. D. Darwin and T. Maguire, *J. Anal. Toxicol.*, 15 (1991) 250.
36 M. R. Harkey, G. L. Henderson and C. Zhou, *J. Anal. Toxicol.*, 15 (1991) 260.
37 D. A. Kidwell, presented at the *36th American Society of Mass Spectrometry Conference on Mass Spectrometry and Allied Topics, San Francisco, CA, June 6–10, 1988.*
38 M. R. Moeller and P. Fey, *Naunyn-Schmiedeberg's Arch. Pharmacol.*, Suppl. 2 to Vol. 344 (1991) R 120.
39 R. M. Martz, *Crim. Lab. Digest*, 15 (1988) 67.
40 R. Martz, B. Donnelly, D. Fetterolf, L. Lasswell, G. W. Hime and W. L. Hearn, *J. Anal. Toxicol.*, 15 (1991) 279.
41 T. Nagai and T. Nagai, *Igaku to Seibutsugaku*, 109 (1984) 145.
42 B. Pelli, P. Traldi, F. Tagliaro, G. Lubli and M. Marigo, *Biomed. Environ. Mass Spectrom.*, 14 (1987) 63.
43 B. A. Goldberger, Y. H. Caplan, T. Maguire and E. J. Cone, *J. Anal. Toxicol.*, 15 (1991) 226.
44 M. R. Moeller and P. Fey, *43th Meeting of the American Academy of Forensic Sciences, Anaheim, CA, Feb., 18 23, 1991*, Abstracts, K45 182.
45 C. A. Sutheimer, *S.O.F.T., News and View*, 27 (1991) 1.
46 A. Viala, E. Deturmeny, C. Aubert, M. Estadieu, A. Durand, J. P. Cano and J. Delmont, *J. Forensic Sci.*, 28 (1983) 922.

47 S. Suzuki, T. Inoue, H. Hori and S. Inayama, *J. Anal. Toxicol.*, 13 (1989) 176.
48 Y. Nakahara, K. Takahashi, M. Shimamine and Y. Takeda, *J. Forensic Sci.*, 36 (1991) 70.
49 S. Balabanova and J. Homoki, *Z. Rechtsmed.*, 98 (1987) 235.
50 H. Brunner, S. Balabanova, J. Homoki and H. U. Wolf, *Beitr. Gerichtl. Med.*, 46 (1988) 127.
51 S. A. Reuschel and F. P. Smith, *J. Forensic Sci.*, 36 (1991) 1179.
52 H. Sachs and H. Brunner, *Beitr. Gerichtl. Med.*, 44 (1986) 281.
53 F. Centini, C. Offidani, A. Carnevale, M. Chiarotti and I. B. Comparini, in G. Piemonte, F. Tagliaro, M. Marigo and A. Frigerio (Editors), *Developments in Analytical Methods in Pharmaceutical, Biomedical and Forensic Sciences*, Plenum Press, New York, 1987, p. 107.
54 E. J. Cone, *J. Anal. Toxicol.*, 14 (1990) 1.
55 H. H. Maurer and Ch. F. Fritz, *Int. J. Leg. Med.*, 104 (1990) 43.
56 H. Sachs, R. Denk and I. Raff, in D. J. Honey and V. J. McLinden (Editors), *Proceedings of the 27th International Meeting, Perth, Oct. 19–23, 1990*, 1992, p. 598.
57 S. Balabanova, P. J. Arnold, H. Brunner, V. Luckow and H. U. Wolf, *Z. Rechtsmed.*, 102 (1989) 495.
58 M. R. Moeller, P. Fey, H. Sachs and F. Kettenbaum, *S.O.F.T. Conference on Hair Analysis for Drugs of Abuse, Washington, DC, May 27–29, 1990*, NIDA Research Monograph Series, in press.
59 I. Raff, R. Denk and H. Sachs, *Z. Rechtsmed.*, 36 (1991) 479.
60 H. Sachs and M. R. Moeller, *Rechtsmedizin*, in preparation.