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Review

Chromatographic procedures for determination of cannabinoids in biological samples, with special attention to blood and alternative matrices like hair, saliva, sweat and meconium

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Abstract

This paper reviews chromatographic procedures for determination of cannabinoids in biological samples. Special attention was focused on blood and alternative matrices like hair, saliva, sweat and meconium. Papers published from 1998 to the early beginning of 1999 were taken into consideration. Gas chromatographic and liquid chromatographic procedures with different detectors (e.g. mass spectrometer or diode array) were considered. Basic information about the biosample assayed, sample preparation, work-up, gas chromatography column or liquid chromatography column and mobile phase, detection mode, reference and validation data are summarized in tables.

Keywords: Reviews; Hair; Saliva; Sweat; Meconium; Cannabinoids

Contents

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1. Introduction

The detection of cannabinoids or other drugs of abuse in urine, the primary goal in the 1980s, has grown to industrial dimensions, mostly due to the availability of immunoassays.

With the development of more specific chromatographic methods, the interest of toxicologists has focused on blood and other alternative biological matrices like hair, saliva, sweat and meconium.

The determination of drugs of abuse in biological matrices has been largely reviewed. In 1992 Bronner and Xu [1] reviewed GC–MS methods for the detection of THC-COOH in biological samples. Much more recently Moeller et al. [2] reviewed the determination of drugs of abuse in blood, Sachs and Kintz [3] reviewed drug testing in hair, Kidwell et al. [4] reviewed determination of drugs in saliva and sweat, and Moore et al. [5] reviewed that determination in meconium. All these reviews have considered papers until the early beginning of 1997.

The number of studies concerning the determination of cannabinoids in biological matrices and particularly in hair has greatly increased over the last 5 years, so that a review focused on cannabis exclusively seems necessary.

1.1. Choice of references

The reviewed references were selected by on-line searching the Medline database. The period from January 1990 to January 1999 was taken into consideration.

2. Occurrence and metabolism

According to the statistical information, cannabis is today the most widely abused illicit drug in the world. Cannabis has been used for its euphoric effects for over 4000 years, Δ-9-tetrahydrocannabinol (THC), the primary psychoactive analyte, is found in the flowering or fruity tops, leaves and resin of the plant. THC with cannabidiol (CBD) and cannabinol (CBN) are the three main constituents presently isolated from the *Cannabis sativa* plant (Fig. 1). In man THC is extensively metabolized in its two main metabolites: 11-nor-9-carboxy-Δ-9-tetrahydrocannabinol see (THC-COOH) and 11-hydroxy-9-Δ-9-tetrahydrocannabinol see (OH-THC) are detectable in biological matrices. Only the hydroxy-metabolite has a psychoactive effect.

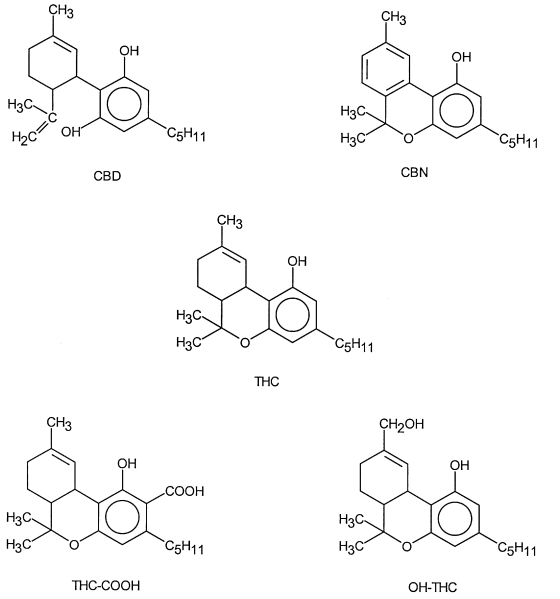

Fig. 1. Structures of the main constituents (THC, CBD, CBN) isolated from the *Cannabis sativa* plant and their two major metabolites.

In blood, beside THC itself, THC-COOH is the species detected in the highest concentration. Determination of the primary psychoactive component (THC) is absolutely necessary in the cases of driving under the influence of drugs [6]. Mathematical models were described for the prediction of time of marijuana use from the analysis of a single plasma sample [7,8]. The models were derived from cannabinoid data obtained from a controlled study of acute marijuana smoking. Predictions of time of exposure were generally accurate, but tended to overestimate time immediately after smoking and tended to underestimate later times.

In hair, THC is the major species and THC-COOH is detectable only at very low concentrations. The weak incorporation rate of THC-COOH in hair is not surprising, taking into consideration the three main factors which influence drug incorporation in hair

(lipophilicity, melanine affinity and membrane permeability). THC-COOH is less incorporated into hair than basic drugs, as membrane permeability is based on the pH gradient between blood at pH 7.4 and hair matrix at pH <5 [9,10].

In contrast to other biological matrices, CBD and CBN have also been detected in significant concentrations in hair samples [11–13].

For saliva, very little is known about the presence of cannabinoids in this matrix and controversial issues are reported in the literature. The presence of THC in saliva could be attributed to contamination of the oral cavity during the smoking process. Only very low concentrations of cannabidiol were observed in saliva, while neither THC-COOH nor OH-THC were detected in any study [14] excepted by Schramm et al. [15].

In sweat, only THC in the low concentration range can be identified and THC-COOH has never been tested positive [16].

A complete study by El Sohly and Feng [17] has demonstrated that THC is absent from meconium and that a larger amount of OH-THC is present in comparison with THC-COOH.

According to the relative abundance of cannabinoids (Fig. 2) chromatographic procedures have to be adapted to each biological matrix.

3. Determination of cannabinoids in biological matrices

3.1. Blood

Table 1 provides a summary of gas chromatographic and liquid chromatographic methods for the determination of cannabinoids in blood.

3.1.1. Gas chromatographic methods (GC)

The authors used two types of extraction methods, either liquid–liquid (LLE) or solid-phase (SPE) extraction. *N*,*O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA) is one of the main derivatization agents used and analysis is usually performed in the electron-impact single-ion monitoring (EI-SIM) mode. Goodall and Basteyns [18] presented a sensitive and reliable method. Samples were screened by fluorescence polarization immunoassays and the analysis was completed on a benchtop mass selective detector using BSTFA and the SIM mode. They obtained very interesting limits of detection, respectively, 0.2 and 2 ng/ml for THC and THC-COOH. Sample stability was also studied over a period of 6 months. Kemp et al. [21] presented a parent method, which allowed to determine THC and six of its metabolites. The limit of detection was similar to the previous

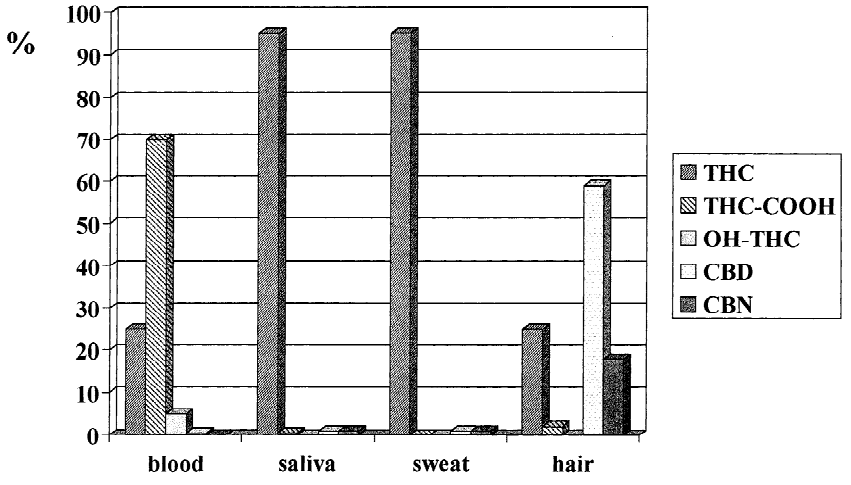

Fig. 2. Relative abundance of cannabinoids in biological matrices.

Table 1
Methods for the determination of cannabinoids in blood

Year	Sample	Compound	Extraction	Derivatization	Column	Detection mode	LOD (ng/ml)	Refs.
(a) *Gas chromatographic methods*								
1991	Plasma	THC	LLE	TFA	SPB-5	NCI-MS	0.08	[23]
		THC-COOH					0.10	
1992	Blood	THC/OH-THC	LLE	MeOH/BF3	HP-5	NCI-MS	0.5/0.5	[24–26]
		THC-COOH		TFA			0.5	
1992	Serum	THC	SPE	TMAH/DMSO	HP-1	EI-SIM	0.3	[20]
		THC-COOH		Iodomethane			3.0	
1993		THC	SPE	Tri-Sil TBT	HP-5	MS–MS	0.1	[22]
		OH-THC					0.02	
1995	Plasma	THC	LLE	BSTFA	HP-5	EI-SIM	1.6/0.9	[21]
		THC-COOH					0.6	
		CBD/CBN					2.1/0.6	
1995	Blood	THC/OH-THC	SPE	BSTFA	CP-SIL5	EI-SIM	Not given	[19]
		THC-COOH						
1995	Blood	THC/OH-THC	LLE	BSTFA	HP-1	EI-SIM	0.2/0.2	[18]
		THC-COOH					2.0	
1996	Blood	THC	LLE	TMAH/DMSO	HP-5MS	EI-SIM	<1.0	[27]
		THC-COOH					<0.5	

Year	Sample	Compound	Extraction	Mobile phase	Column	Detection mode	LOD (ng/ml)	Refs.
(b) *Liquid chromatographic methods*								
1993	Blood	THC	LLE	ACN–MeOH–	Spherisorb	ED	1.0	[28]
		OH-THC		sulfuric acid	C8		1.0	
1995	Blood	THC	SPE	ACN–H_2O–	Lichrosorb	ED	2.5	[19]
		THC-COOH		sulfuric acid	RP8		1.0	
1995	Blood	THC	SPE	ACN–H_2O–	Lichrosorb	UV	20	[19]
		THC-COOH		sulfuric acid	RP8		1	

method for THC-COOH and a little bit higher for THC.

The combination of GC and tandem mass spectrometry (MS–MS) further improved the sensitivity 10- to 100-fold compared to SIM methods. Nelson et al. [22] described the application of solid-phase extraction (SPE) and GC–MS–MS method for the detection of THC and OH-THC in plasma, down to limits of detection of 0.01 and 0.02 ng/ml, respectively.

Several authors [24,25] used trifluoroacetyl derivatives and negative chemical ionization (NCI) detection method. This method was first introduced by Foltz et al. [26] already in 1983. Very low limits of detection were achieved with this kind of techniques. Shaw et al. [23] measured THC and THC-COOH using a high-energy dynode detector system, retrofilled to a GC–MS system operating in the NCI mode. They improved their limit of detection for THC in plasma by about 6-fold over that obtained with the same GC–MS system without the new detector (0.08 vs. 0.5 ng/ml).

Since the trimethylsilylation technique is subject to hydrolysis after several hours [29], other derivatization agents were presented for routine work. Moeller et al. [20], using iodomethane and tetramethylammonium hydroxide (TMAH) as derivatization agents, quantitated THC and THC-COOH simultaneously in serum. The extraction was carried out by SPE. They obtained interesting limits of detection, 0.3 and 3.0 ng/ml, respectively, for THC and THC-COOH. Four years later, Kintz et al. [27] proposed a method using the same derivatization agent and a liquid–liquid extraction (LLE) with hexane–ethyl acetate. The limits of quantification were, respectively, 1.0 and 0.5 ng/ml for THC and

THC-COOH. For forensic purposes, these limits of quantification seem generally useful.

N-Methyl-*N*-*tert.*-butyldimethylsilyltrifluoroacetamide (MTBSTFA) was employed as derivatization reagent by Clouette et al. [29] and Moore et al. [30] for the analysis of THC-COOH in urine and meconium samples. Since the advantage of this reagent lies in the formation of unusually stable derivatives of THC-COOH (over a period of 10 days), no paper presenting the use of this reagent for analysis of blood was found in the review time frame.

3.1.2. Liquid chromatographic methods (LC)

Detection of cannabinoids using LC procedures is rare. Only three papers about analysis in blood could be found in the literature. Table 1 summarizes important data of these papers. Gerostamoulos and Drummer [28] developed a HPLC method using electrochemical detection (ED). The detection limits for THC and OH-THC were 1 ng/ml. Abdul Rahman et al. [19] used several extraction methods and concluded that acetonitrile deproteinization, followed by solid-phase extraction gave the cleanest extract and the best recoveries. Comparison between HPLC (with UV and ED detection) and GC–MS (EI-SIM) showed advantages for the latter method because of its better sensitivity and specificity.

3.2. Hair

As mentioned before, THC is a species detected in hair and THC-COOH is detectable only at very low concentrations. No LC method for the determination of cannabinoids in hair was found in the literature. Twelve GC procedures are given in Table 2.

In the early 1990s, three methods were published. These methods allowed the quantification of THC and THC-COOH separately. But in 1995, Cirimele et al. [35] and Jurado et al. [36] reported the first GC–MS methods, allowing the determination of THC and THC-COOH in the same run. The first procedure was specially dedicated to cannabis, while the second was included in a general screening for opiates, cocaine and cannabis.

In contrast to blood, no procedure including BSTFA as derivatization agent was published and

Table 2
Methods for the determination of cannabinoids in hair

Year	Compound	Extraction	Derivatization	Column	Detection mode	LOD (ng/mg)	Refs.
1992	THC-COOH	1 *M* NaOH and SPE	TFA	?	EI-SIM	<0.4	[31]
1992	THC-COOH	2 *M* NaOH and SPE	PFPA/PFPOH	HP-1	EI-SIM	Not given	[32,33]
1993	THC	MeOH	PFPA/PFPOH	?	EI-SIM	0.01	[34]
1995	THC THC-COOH	1 *M* NaOH and LLE	PFPA/PFPOH	HP-5MS	EI-SIM	0.1	[35]
1995	THC THC-COOH	11.8 *M* KOH and LLE	HFBA/HFIP	HP-1	EI-SIM	0.05 0.04	[36]
1995	THC-COOH	1 *M* NaOH and LLE	PFPA/PFPOH	HP-1	NCI-MS	0.005	[37]
1995	THC/OH-THC THC-COOH	1M NaOH and LLE	TFAA/MeOH /BF3	Restek 200-15M	NCI-MS	0.05/0.5 0.05	[38]
1995	THC-COOH	10 *M* NaOH and LLE	HFBA/HFIP	DB-5MS	MS–MS-NCI	0.00002	[39,40]
1996	THC	MeOH	PAA	DB-1	EL-SIM	0.1	[43]
1996	THC CBN/CBD	1 *M* NaOH and LLE	No	HP-5MS	EL-SIM	0.1 0.01/0.02	[42]
1997	THC-COOH	10 *M* KOH and SPE	PFPA/HFIP	DB-5	MS–MS-NCI	<0.0002	[41]
1999	THC CBN/CBD	1 *M* NaOH and SPME	No	HP-5MS	EI-SIM	0.1 0.1/0.2	[13]

the main derivatization agents used were the fluoroacetyl derivatives.

As the measured concentrations were very low, some authors suggested the use of NCI to target the drugs [37,38]. The combination of NCI and tandem mass spectrometry improved the sensitivity 100-fold compared to SIM methods [39–41].

Recently Cirimele et al. [11] developed a simple method, based on the simultaneous determination of cannabinol (CBN), cannabidiol (CBD) and THC. This procedure should be used as a screening method, since it is rapid, economic and does not require derivatization before the analysis by GC–MS.

The preparation of hair should be summarized as the following: after decontamination with various mixtures (organic or aqueous solvents), the hair samples are generally hydrolyzed in a strongly alkaline medium to obtain complete dissolution of the matrix. Then the hair digest is extracted either by LLE or by SPE. Finally the extract is derivatized before analysis by GC–MS.

However, extraction of THC was also proposed using methanol sonication [34,42] and supercritical fluid extraction [43]. Very recently Strano-Rossi and Chiarotti [13] described a new application of solid-phase microextraction (SPME) to cannabis testing in hair. Fifty milligrams of hair were decontaminated with petroleum ether, hydrolyzed with NaOH and submitted to SPME. Then the SPME extract was analyzed by GC–MS. The limit of detection was 0.1 ng/mg for CBN and THC, 0.2 ng/mg for CBD. This method could be considered as the most rapid screening method for cannabinoids in hair.

3.3. Saliva

Very little is known about the composition of cannabinoid compounds in saliva and controversial issues are reported in the literature [4,44]. The presence of THC in saliva could be caused by contamination of the oral cavity during the smoking process.

Therefore, analytical methods focused on the detection of THC in saliva using GC–MS [45,46] and coupling tandem immunoaffinity chromatography with high-performance liquid chromatography [47].

More recently Hall et al. [48] described application of SPME to cannabis testing in saliva. Saliva specimens for SPME quantitation were treated in the following manner: to 1 ml of saliva, 1 ml of deionized water and 0.5 ml of acetic acid were added during stirring. The limits of detection were 1 ng/ml for CBD, CBN and THC with a signal-to-noise ratio, respectively, of 12, 80 and 15. In one analysis of a marijuana smoker's saliva, only THC and a trace of CBN were detected. In other studies, neither THC-COOH nor OH-THC were detected [44], excepted that by Schramm et al. [15] using high-performance liquid chromatography and thermospray mass detection.

3.4. Sweat

Numerous methods have been developed to induce sweat and to collect samples from human skin [4]. Patches have been developed to wear for extended periods and methanol (or another solvent) was used to eluate drugs from the pad.

Ion trap MS–MS was reported as useful for cannabis in sweat [49]. Only THC, in the low ng/patch range could be determined and THC-COOH was never detected in sweat.

3.5. Meconium

The determination of cannabinoids in meconium poses difficult analytical problems due to the small amounts present [5].

A publication by Moore et al. [30] presented the determination of THC-COOH in meconium. Following homogenization of the meconium in methanol and the addition of 11.8 *M* potassium hydroxide, the sample was allowed to stand for 15 min. After centrifugation, deionized water was added to the supernatant and the specimen was extracted with hexane–ethyl acetate. After back extraction into concentrated hydrochloric acid, the solvent was evaporated to dryness and the *tert*.-butyl-dimethylsilyl derivative of THC-COOH was formed by using MTBSTFA as the derivatizing agent. The advantages of this agent have already been presented in this review [29]. Analysis was performed in the EI-SIM mode and the limit of detection was 2 ng/g. A second publication was designed by El Sohly and

Feng [17] to investigate THC, THC-COOH, OH-THC and its 8-OH metabolites after enzymatic hydrolysis of meconium extracts.

The authors suggested that THC-COOH is significantly glucuronide bound in meconium and demonstrated that THC and its 8-OH metabolites are absent, and a larger amount of OH-THC in comparison with THC-COOH.

Kudo et al. [50] proposed a method for the analysis of THC not specially in meconium but in tissue samples. Derivatization was performed with iodomethane and tetrabutylammonium hydroxide (TBAH), followed by detection in the EI-SIM mode. Under those conditions the LOD was 1 ng/g.

4. Conclusions

In the last 10 years, with the development of more specific chromatographic methods, the interest of toxicologists has focused on blood and other alternative biological matrices like hair, saliva, sweat and meconium.

The relative abundance of cannabinoid compounds varies with the type of the biological matrix:

- in blood, THC-COOH is the major species and THC is detectable at lower concentrations;
- in saliva and sweat, only THC is detectable and the presence of other metabolites is rare;
- in hair, CBN, THC and CBD are the three major cannabinoid compounds and THC-COOH is detectable only at very low concentrations; and
- in contrast to other biological matrices, in meconium only THC-COOH is detectable.

Extensive developments in derivatization procedures, resulting in significant advances, have been made in the last 10 years. Therefore, GC–MS is the method of choice for the identification and quantitation of cannabinoids in all of these investigated biological matrices.

Numerous liquid–liquid and solid-phase extractions are presented and often the choice of the best method is difficult.

Finally solid-phase microextraction (SPME) is a very attractive method for biological matrices like saliva, sweat and hair digest and should play an important role as a screening method. Coupled with GC–MS, it is an efficient technique for the detection of cannabinoids in biological matrices due to its specificity and sensitivity.

5. List of abbreviations

ACN	acetonitrile
BSTFAN	*O*-bis(trimethylsilyl)trifluoroacetamide
CBD	cannabidiol
CBN	cannabinol
CI	chemical ionization
DMSO	dimethylsulfoxide
ED	electrochemical detection
EI	electron-impact ionization
GC	gas chromatography
GC–MS	gas chromatography–mass spectrometry
HFIP	hexafluoroisopropanol
LC	liquid chromatography
LC–MS	liquid chromatography–mass spectrometry
LLE	liquid–liquid extraction
LOD	limit of detection
MeOH	methanol
MS	mass spectrometry
MS–MS	tandem mass spectrometry
MTBSTFA	*N*-methyl-*N*-*tert*.-butyldimethylsilyltrifluoroacetamide
NCI	negative chemical ionization
OH-THC	11-hydroxy-Δ-9-tetrahydrocannabinol
PAA	propionic acid anhydride
PFPA	pentafluoropropionic anhydride
PFPOH	pentafluoro-1-propanol
SIM	single ion monitoring
SPE	solid-phase extraction
SPME	solid-phase microextraction
TBAH	tetrabutyammonium hydroxide
TFAA	trifluoroacetic anhydride
THC	Δ-9-tetrahydrocannabinol
THC-COOH	11-nor-9-carboxy-Δ-9-tetrahydrocannabinol
TMAH	tetramethylammonium hydroxide
UV	ultraviolet

References

[1] W.E. Bronner, A.S. Xu, Chromatographia 580 (1992) 63–75.
[2] M.R. Moeller, S. Steinmeyer, Th. Kraemer, J. Chromatogr. B 713 (1998) 91–109.
[3] H. Sachs, P. Kintz, J. Chromatogr. B 713 (1998) 147–161.
[4] D.A. Kidwell, J.C. Holland, S. Arthanaselis, J. Chromatogr. B 713 (1998) 111–135.
[5] C. Moore, A. Negrusz, D. Lewis, J. Chromatogr. B 713 (1998) 137–146.
[6] H.W.J. Robbe, in: H.W.J. Robbe (Ed.), Influence of Marijuana on Driving, Institute for Human Psychopharmacology, Maastricht, 1994, pp. 1–232.
[7] M.A. Huestis, J.E. Henningfield, E.J. Cone, J. Anal. Toxicol. 16 (1992) 276–282.
[8] M.A. Huestis, J.E. Henningfield, E.J. Cone, J. Anal. Toxicol. 16 (1992) 283–290.
[9] Y. Nakahara, in: Presented at the 2nd International Meeting on Clinical and Forensic Aspects of Hair Analysis in Genoa, Italy, June 6–8, 1994.
[10] V. Cirimele, in: P. Kintz (Ed.), Drug Testing in Hair, CRC Press, Boca Raton, FL, 1996, pp. 181–189.
[11] V. Cirimele, H. Sachs, P. Kintz, P. Mangin, J. Anal. Toxicol. 20 (1996) 13–16.
[12] P. Kintz, V. Cirimele, P. Mangin, in: R.A. de Zeeuw, I. Al Hosani, S. Al Munthiri, A. Magboot (Eds.), Proceedings of the 1995 International Conference and Workshop for Hair Analysis in Forensic Toxicology, Abu Dhabi, Nov. 1995, pp. 194–202.
[13] S. Strano-Rossi, M. Chiarotti, J. Anal. Toxicol. 23 (1999) 7–10.
[14] E.J. Cone, A.J. Jenkins, in: S.H. Wong, I. Sunshine (Eds.), Handbook of Analytical Therapeutic Drug Monitoring and Toxicology, CRC Press, Boca Raton, FL, 1997, pp. 303–333.
[15] W. Schramm, R.H. Smith, P.A. Graig, D.A. Kidwell, J. Anal. Toxicol. 16 (1992) 1–9.
[16] C. Ehorn, D. Fretthold, M. Maharaj, in: Proceedings of the TIAFT-SOFT, Tampa, USA, 1994, Abstract No. 11.
[17] M.A. ElSohly, S. Feng, J. Anal. Toxicol. 22 (1998) 329–335.
[18] C.R. Goodall, B.J. Basteyns, J. Anal. Toxicol. 19 (1995) 419–426.
[19] M.Z. Abdul Rahman, R.A. Anderson, M. MacDonald, K. Williams, in: B. Jacob, W. Bonte (Eds.), Advances in Forensic Science, Vol. vol. 5, Verlag Dr Koester, Berlin, 1995, pp. 289–295.
[20] M.R. Moeller, G. Doerr, S. Warth, J. Forensic Sci. 37 (1992) 969–983.
[21] P.M. Kemp, I.K. Abukhalaf, J.E. Manno, B.R. Manno, D.D. Alford, G.A. Abusada, J. Anal. Toxicol. 19 (1995) 285–291.
[22] C.C. Nelson, M.D. Fraser, J.K. Wilfahrt, R.L. Foltz, Ther. Drug Monit. 15 (1993) 557–562.
[23] L.M. Shaw, J. Editing-Owens, R. Maltes, Clin. Chem. 37 (1991) 2062–2068.
[24] D.E. Moody, L.F. Rittenhouse, K.M. Monti, J. Anal. Toxicol. 16 (1992) 297–301.
[25] D.E. Moody, K.M. Monti, D.J. Crouch, J. Anal. Toxicol. 16 (1992) 302–306.
[26] R.L. Foltz, K.M. McGinnis, D.M. Chinn, Biomed. Mass Spectrom. 10 (1983) 316–323.
[27] P. Kintz, V. Cirimele, G. Pepin, P. Marquet, M. Deveaux, P. Mura, Toxicorama 8 (1996) 29–33.
[28] J. Gerostamoulos, O.H. Drummer, J. Forensic Sci. 38 (1993) 649–656.
[29] R. Clouette, M. Jacob, P. Koteel, M. Spain, J. Anal. Toxicol. 17 (1993) 1–4.
[30] C.M. Moore, J.W. Becker, D.E. Lewis, J.B. Leikin, J. Anal. Toxicol. 20 (1996) 50–51.
[31] P. Kintz, B. Ludes, P. Mangin, J. Forensic Sci. 37 (1992) 328.
[32] M.R. Moeller, P. Frey, H. Sachs, Forensic. Sci. Int. 63 (1993) 43–53.
[33] M. Moeller, J. Chromatogr. 580 (1992) 125–134.
[34] G. Kauert, Z. Rechtsmed. 40 (1993) 229.
[35] V. Cirimele, P. Kintz, P. Magnin, Forensic Sci. Int. 70 (1995) 175–182.
[36] C. Jurado, M.P. Giménez, M. Ménendez, M. Repetto, Forensic Sci. Int. 70 (1995) 165–174.
[37] P. Kintz, V. Cirimele, P. Magnin, J. Forensic Sci. 40 (1995) 619–623.
[38] D. Wilkins, H. Haughey, E. Cone, M. Huestis, R. Foltz, D. Rollins, J. Anal. Toxicol. 19 (1995) 483–491.
[39] T. Cairns, D.J. Kippenberger, H. Scholtz, W.A. Baumgartner, in: R.A. de Zeeuw, I. Al Hosani, S. Al Munthiri, A. Magbool (Eds.), Proceedings of the 1995 International Conference and Workshop for Hair Analysis in Forensic Toxicology, Abu Dhabi, Nov. 1995, pp. 185–193.
[40] T. Mieczkowski, Forensic Sci. Int. 70 (1995) 83–91.
[41] M. Uhl, Forensic Sci. Int. 84 (1997) 281–294.
[42] G. Kauert, J. Röhrich, Int. J. Legal Med. 108 (1996) 294–299.
[43] V. Cirimele, P. Kintz, R. Majdalani, P. Mangin, J. Chromatogr. B 673 (1995) 173–181.
[44] E.J. Cone, A.J. Jenkins, in: S.H. Wong, I. Sunshine (Eds.), Handbook of Analytical Therapeutic Drug Monitoring and Toxicology, CRC Press, Boca Raton, FL, 1997, pp. 303–333.
[45] D.B. Menkes, R.C. Howard, G.F.S. Spears, E.R. Cairns, Psychopharmacology 103 (1991) 277–279.
[46] P. Kintz, V. Cirimele, Biomed. Chromatogr. 11 (1997) 371.
[47] V. Kircher, H. Parlar, J. Chromatogr. B 677 (1996) 245.
[48] B.J. Hall, M. Satterfield-Doerr, A.R. Parikh, J.S. Brodbelt, Anal. Chem. 70 (9) (1998) 1788–1796.
[49] C. Ehorn, D. Fretthold, M. Maharaj, in: Proceedings of the TIAFT-SOFT, Tampa, USA, 1994, Abstract No. 11.
[50] K. Kudo, T. Nagata, K. Kimura, T. Imamura, N. Jitsufuchi, J. Anal. Toxicol. 19 (1995) 87–90.