JrnlID 216_ArtID 1209_Proof# 1 - 24/02/2007

Anal Bioanal Chem
DOI 10.1007/s00216-007-1209-z

REVIEW

Bioanalytical procedures for detection of chemical agents in hair in the case of drug-facilitated crimes

Pascal Kintz

Received: 5 January 2007 / Revised: 9 February 2007 / Accepted: 14 February 2007

Abstract The use of a drug to modify a person's behavior for criminal gain is not a recent phenomenon. However, the recent increase in reports of drug-facilitated crimes (sexual assault, robbery) has caused alarm in the general public. The drugs involved can be pharmaceuticals, such as benzodiazepines (flunitrazepam, lorazepam, etc.), hypnotics (zopiclone, zolpidem), sedatives (neuroleptics, some anti-H1) or anaesthetics (γ-hydroxybutyrate, ketamine), drugs of abuse, such as cannabis, ecstasy or LSD, or more often ethanol. To perform successful toxicological examinations, the analyst must follow some important rules: (1) obtain as soon as possible the corresponding biological specimens (blood and urine); (2) collect hair about 1 month after the alleged event; (3) use sophisticated analytical techniques (gas or liquid chromatography coupled to tandem mass spectrometry, MS/MS, headspace gas chromatography); and (4) take care in the interpretation of the findings. Drugs used to facilitate sexual assaults can be difficult to detect (active products at low doses, chemical instability), possess amnesic properties and can be rapidly cleared from the body (short half-life). In these situations, blood or even urine can be of low interest. This is the reason why some laboratories have developed an original approach based on hair testing. Hair was suggested as a valuable specimen in situations where, as a result of a delay in reporting the crime, natural processes have eliminated the drug from typical biological specimens. While there are a lot of papers that have focused on the identification of drugs in hair following chronic drug use, those dealing with a single dose are very scarce. The experience of the author and a review of the existing literature will be presented for cases involving benzodiazepines, hypnotics, γ-hydroxybutyrate and various sedatives or chemical weapons. The expected concentrations in hair are in the low picogram/milligram range for most compounds. Hair analysis may be a useful adjunct to conventional drug testing in sexual assault. It should not be considered as an alternative to blood and urine analyses, but as a complement. This approach may find useful applications, but the definition of legally defensible cutoff values would require much more data. MS/MS technologies appear as a prerequisite in drug-facilitated cases.

Keywords Hair · Drug-facilitated crime · Drug-facilitated sexual assault · Liquid chromatography–mass spectrometry

P. Kintz (✉)
Laboratoire ChemTox,
3 rue Gruninger,
67400 Illkirch, France
e-mail: pkintz@labochemtox.com

Introduction

In the last few years, considerable information about drug-facilitated crimes (rape, sexual assault, robbery, sedation of elderly persons) has accumulated. In these situations, the victims are subjected to nonconsensual acts while they are incapacitated through the effects of a drug. This impairs their ability to resist or to give consent to the act. In a typical scenario, a predator (rapist, robber) surreptitiously spikes a drink of an unsuspecting person with a hypnotic drug. Victims, both women and men, usually report loss of memory during and after the event. For the perpetrator, the ideal substance is one that is readily available, is easy to administer, rapidly impairs consciousness and causes

anterograde amnesia (i.e., it prevents the recall of events that occurred whilst under the influence of the drug, but not general memory).

The most commonly encountered drugs in alleged drug-facilitated crimes (DFC) are ethanol (alcohol), cannabis and to a lesser extent cocaine and MDMA. Pharmaceuticals have also been observed though to a lesser degree [1, 2]. The drugs involved can be benzodiazepines (flunitrazepam, lorazepam, etc.), hypnotics (zopiclone, zolpidem), sedatives, neuroleptics, some histamine H1 antagonists or anesthetics (γ-hydroxybutyrate or GHB, ketamine). Owing to their low dose, except for GHB, a surreptitious administration into beverages such as coffee, soft drinks (cola) or, even better, alcoholic cocktails is relatively simple.

Blood and urine are the conventional specimens to document drug exposure [3]. The narrow window of detection of GHB, 6 and 10 h in blood and urine, respectively, is an example of the current limitation of these specimens to demonstrate exposure after late sampling [4]. For all compounds involved in DFC, the detection times in blood and urine depend mainly on the dose and sensitivity of the method used. Prohibiting immunoassays and using only hyphenated techniques, we can find substances in blood for 6 h to 2 days and in urine for 12 h to 5 days [5]. Sampling blood or urine is of low interest 48 h after the offense occurred. To address a response to this important caveat, hair was suggested as a valuable specimen. Hair sampling is a useful complement to these analyses to increase the window of detection and to permit differentiation of a single exposure from chronic use of a drug by segmentation. Moreover, owing to the long delays that are frequently encountered between the event and the matter being reported to the police, hair can often be the only matrix capable of providing corroborative evidence of a committed crime.While there are a lot of papers that have focused on the identification of drugs (mainly drugs of abuse) in hair following chronic use, those dealing with a single dose are very scarce.

This paper presents the analytical strategy in DFC investigation using hair as the key matrix.

Hair collection and procedure

Hair is best collected from the area at the back of the head, called the vertex posterior. Compared with other areas of the head, this area has less variability in the hair growth rate, the number of hairs in the growing phase is more constant and the hair is less subject to age-related and sex-related influences. Hair strands are cut as close as possible to the scalp, and the location root-tip must be mentioned. Storage is achieved at ambient temperature in aluminum foil, an envelope or a plastic tube.

Our laboratory recommends waiting for 4–5 weeks after the offense and then collecting four strands of about 100 hairs. One strand will be used to test for drugs of abuse (mostly for cannabis, but sometimes for ecstasy-related compounds and cocaine), one for GHB and another one for a screening of hypnotics. The last strand is collected for a potential counteranalysis. Assuming normal hair growth rate (range from 0.7 to 1.4 cm/month with a mean of about 1 cm/month accepted by the scientific community), it is the opinion of the author to cut the strand into three segments of 2 cm in order to document any drug-facilitated sexual assault case. Administration of a single dose would be confirmed by the presence of the drug in the proximal segment (root), with no detection in the other segments. This approach is now internationally accepted by the active scientists involved in the field.

GHB analysis

Although considered as a drug of abuse, GHB has been used clinically since the 1960s as an intravenous anesthetic. It was also investigated for treatment of insomnia, of alcohol and opiates withdrawal syndrome and in cerebrovascular disorders. The purported enhancement of sexuality, coupled with a possible abrupt coma-inducing effect, ease of administration in spiked drinks and potential amnesia has resulted in the use of GHB as an assault-related drug. GHB is also attractive to rapists as it is readily available (i.e., Internet, on the street, in dance clubs or fitness centers). Authentic GHB-facilitated rapes are infrequent, but the number of requests to test for the drug is high.

Given the short half-life of the drug, hair is presented as the solution to document GHB exposure in DFC. Only two papers [6, 7] have been published on this topic, both using roughly the same procedure, based on gas chromatography (GC) coupled to tandem mass spectrometry (MS/MS).

Briefly, hair is decontaminated and then cut into 3-mm segments over a length of 3 cm (ten segments). About 5–10 mg of decontaminated hair is incubated overnight in 0.01 N NaOH at 56 °C, in the presence of 10 ng GHB-d_6 used as an internal standard. After cooling, the homogenate is neutralized with HCl and the drugs are extracted with ethyl acetate and finally silylated with bis(trimethylsilyl) trifluoroacetamide and 1% trimethylchlorosilane . GHB and the internal standard are separated on a nonpolar capillary column and detected by MS/MS.

Endogenous concentrations are generally lower than 2 ng/mg. This was confirmed by an independent study [8]. Since GHB is present in the hair of the general population under physiological concentrations, toxicologists must be able to discriminate between endogenous levels and a concentration resulting from exposure. The

implementation of a cutoff concentration must be done cautiously, owing to the wide distribution of endogenous concentrations, from 0.5 to 12.0 ng/mg. The solution is to use each subject as his/her own control. From the demonstration that physiological concentrations are stable along the hair shaft, except at the root part, one can suppose that exposure will lead to a peak concentration that can be detected. Use of MS/MS is mandatory because of the low amount of hair that needs to be tested as a consequence of the short 3-mm segments that need to be analyzed.

Hair strands were obtained from a 19-year-old girl who claimed to have been sexually assaulted after drinking a soft drink spiked with a drug. She had no memory of the crime and went to the police 5 days after the alleged rape. After contact with the police, our laboratory recommended waiting for about 1 month in order to have the corresponding growing hair between the root and the tip. Full-length hair samples (8 cm long) were taken at the surface of the skin from the vertex and stored in plastic tubes at room temperature. Segmentation revealed an increase of GHB concentrations at the corresponding time (Fig. 1) to 2.4 and 2.7 ng/mg, confirming exposure, when compared with basal physiological concentrations around 0.7 ng/mg. The rapist, who was arrested several days after the assault, did not challenge this result.

Benzodiazepines and hypnotics analysis

Major progress in the detection in hair of a single dose of benzodiazepines or hypnotics is a result of the use of liquid chromatography (LC) coupled to MS/MS in forensic laboratories. Two French authors are associated with these procedures, namely, Villain and Chèze, as they have written most of the literature, with comparative strategy. Later, Laloup et al [9] offered a screening procedure and some alternatives (extraction with 1-chlorobutane, mobile phase of methanol and formate buffer), with quite the same limits of quantitation.

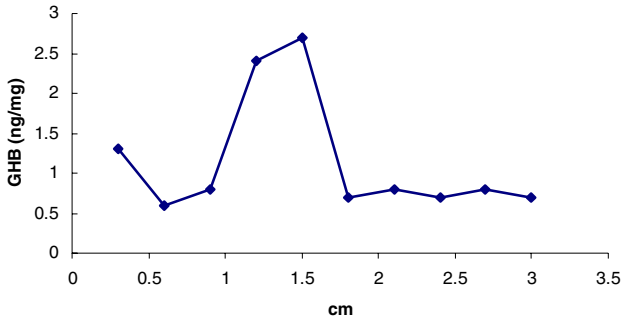

Fig. 1 γ-Hydroxybutyrate (*GHB*) segmental analysis in the hair of a victim raped under the influence of the drug

Villain et al. have published a series of papers, including a general screening procedure [10] and specific methods for bromazepam [11], zolpidem [12, 13], zopiclone [14] and alprazolam [15]. The authors failed to identify lorazepam in hair after a single exposure [16]. Chèze et al. [17] published a procedure to test for bromazepam and clonazepam.

Key points of the analysis are as follows. After decontamination of the hair, the strand is segmented and cut into small pieces. About 20 mg is incubated overnight in phosphate buffer (pH 7.6 or 8.4), in the presence of diazepam-d_5 or clonazepam-d_4 used as internal standards, and is extracted by dichloromethane/diethyl ether (90:10, v/v) or only dichloromethane. For separation, Villain et al. and Laloup et al. used an XTerra MS C18 column (3.5 µm, 100 mm×2.1-mm inner diameter), while Chèze et al. used an Uptisphere ODB column (5 µm, 150 mm×2.1-mm inner diameter). In all cases, detection was achieved by a tandem mass spectrometer equipped with an ionspray atmospheric pressure interface. For identification, Villain et al. used two precursor ion/product ion transitions for each drug. Chéze et al. used three transitions, while Laloup et al. proposed screening using one transition and then further confirmation of the identity of the compounds through a second injection of positive samples, monitoring two transitions per compound.

More details of the screening procedure of Villain et al. can be found below. The method provides good resolution of the different drugs. The limit of quantification for all benzodiazepines and hypnotics ranges from 0.5 to 5 pg/mg using a 20-mg hair sample. The method is linear in hair for each compound, from the limit of quantification to 200 pg/mg (r^2>0.99). Precisions and accuracies, at 10 and 50 pg/mg, were less than 20% in all cases but one. The extraction recovery, measured at the same two concentrations, ranged from 32 to 76%, which is suitable for a screening procedure.

In case of nitrobenzodiazepines, the target compound is the 7-amino metabolite. Owing to their stability in alkaline medium, in contrast with other benzodiazepines, it is possible to lower their limit of quantification about 5 times with a specific extraction after sodium hydroxide hydrolysis [17].

Detected concentrations are in the range 1–30 pg/mg, depending on the drug administered.

A 39-year old woman, in trouble with her husband, felt sleepy for 24 h after having consumed a cup of coffee, at home. A blood sample, collected 20 h after absorption, revealed the presence of 51 ng/mL bromazepam, whereas hair sampled at the same time was bromazepam-free. Another strand of hair was collected 1 month after the event and the proximal 2 cm-long segment tested positive for bromazepam at 10.3 pg/mg and the other segments (2–4 and 4–6 cm) still tested negative. These results are consistent with a single exposure to this drug. The analysis

of the residue in the cup of coffee (tested positive for bromazepam) and the husband's declaration did not challenge the biological conclusions.

A 42-year-old man was offered a drink by a relative during a party. Several hours later, he noticed that his money was gone, with no recollection of the event during the previous period. He went to the police, but no specimen was collected at that time. After several similar cases in the same region of France, the judge in charge of the case asked us to perform a hair test. 7-Aminoflunitrazepam, the major metabolite of flunitrazepam and its marker in hair, was detected in the corresponding segment of hair at 31.7 pg/mg, while the distal segment tested negative.

Miscellaneous drugs

In most cases, benzodiazepines are identified in hair in cases of DFC. However, some unusual compounds can be observed. This is also because the imagination of the perpetrator has no limit.

Thiopental

Frison et al. [18] detected thiopental (150–300 pg/mg) and its metabolite pentobarbital (200–400 pg/mg) in three different proximal segments, corresponding to the time of the assault, while distal segments tested negative. Hair was analyzed by means of solid-phase microextraction and GC–multiple MS (ion trap). Pubic hair also tested positive for both drugs.

Glibenclamide

Villain et al. [19] detected glibenclamide, an antidiabetic agent in an intrafamily situation. A 30-year-old man, was admitted to hospital after having consumed several beers, at home, the previous night. He had glycemia at home with a glucose level of 0.33 g/l. The emergency unit treated him with a perfusion of diazepam and 30% glucose, but hypoglycemia persisted at a glucose level of 0.40 g/l. Despite intensive resuscitation attempts, vegetative coma occurred rapidly. Five months later, the patient was pronounced dead. A blood sample, collected on admission, revealed the presence of 41 ng/ml glibenclamide. To discriminate between a single administration and repetitive administration, the laboratory was requested to analyze a hair strand. A 4-cm-long hair was divided into two 2-cm segments, and incubated in a pH 5.5 buffer in presence of gliclazide, used as an internal standard. Drugs were extracted by a mixture of dichloromethane/diethyl ether (50:50) and were subjected to LC-MS/MS using an XTerra MS C18 column. Both hair segments tested positive at 23 and 31 pg/mg.

Clozapine

Bartsch et al. [20] published a case where clozapine was identified in Munchausen syndrome by proxy, which can be considered as a special situation of DFC. Multiple exposure to clozapine was revealed after incubation with buffer at pH 7.4 and clean-up of the aqueous phase by solid-phase extraction, followed by GC-MS. The measured concentration of clozapine in the hair of a 1-year-old child after exhumation was 3.2 ng/mg.

α-Chloralose

Sporkert et al. [21] reported on a 36-year-old man taken to the Institute of Legal Medicine for an autopsy. Before his death, the deceased had been hospitalized several times after an epilepsy-like crisis. Despite clinical examination (EEG, NMR), an epileptogenic focus was not detectable. Autopsy findings as well as results of neurological examination could not explain the cause of death.

Hair analysis was carried out in order to verify whether the epilepsy-like symptoms could be explained by repeated administration of α-chloralose that was found in the blood. For this purpose, a GC-MS detection method was developed. Because of its similar chemical properties to the analyte during and after derivatization, methyl-α-glucopyranose was chosen as an internal standard. Hair was extracted with a methanol/water mixture (80:20) for 14 h at 50 °C. After evaporation of the extraction solvent, the residue was derivatized with trifluoroacetic anhydride. Mass-spectrometric measurements in SCAN and SIM modes were carried out using negative chemical ionization (NCI) with methane as the reagent gas. Owing to the high number of halogen atoms in the molecule, a high NCI sensitivity could be achieved with a limit of quantification of 10 pg/mg for α-chloralose. Segmental hair analysis yielded α-chloralose concentrations in the range from 75 to 139 ng/mg for each segment, suggesting repetitive exposure to α-chloralose. The results of hair analysis supported the assumption of the police that the man had been exposed to and poisoned by this rarely used rodenticide.

Niaprazine

Pépin et al. [22] reported the case of six children that were under the supervision of a nurse. To make them quiet, she

repetitively administered niaprazine, a hypnotic. The drug was extracted at pH 7.6 using diethyl ether and detected by ion-trap LC-MS/MS. Measured concentrations were in the range 4.5–46.9 ng/mg.

Scopolamine

Kintz et al. [23] developed a procedure to test scopolamine by ultraperformanceLC-MS/MS in the hair of three children after alleged exposure to Feminax®. This pharmaceutical, commercialized in England, contains active ingredients such as paracetamol, codeine, caffeine and scopolamine and is proposed for the treatment of headache, dental pain, related pain and menstrual cramps.

A strand of hair, collected from each child, was decontaminated using dichloromethane, and then segmented (three segments of 2 cm for the first two subjects and two segments of 2.5 cm for the third). The segments were pulverized and incubated overnight in pH 8.4 phosphate buffer in the presence of atropine-d_3, used as an internal standard. Liquid–liquid extraction with dicloromethane/2-propanol/*n*-heptane (50:17:33, v/v/v) was used.

The analysis of each hair segment showed the following concentrations of scopolamine:

- Subject 1: 0–2 cm, 0.7 pg/mg; 2–4 cm, 0.4 pg/mg; 4–6 cm, less than 0.2 pg/mg
- Subject 2: 0–2 cm, 0.6 pg/mg; 2–4 cm, 0.3 pg/mg; 4–6 cm, less than 0.2 pg/mg
- Subject 3: 0–2.5 cm, 0.3 pg/mg; 2.5–5 cm, 1.1 pg/mg

Figure 2 is a typical chromatogram of a hair extract, showing the great sensitivity of the procedure.

Furthermore, codeine (89–544 pg/mg) was identified in each segment, which confirms the children's repetitive exposure to Feminax®.

The combination of scopolamine and codeine was used to sedate the children by the parents, who did not challenge the toxicology results.

Alimemazine

The first cases involving repetitive sedation linked to the use of trimeprazine as a DFC and subsequent impairment of two children were reported by Kintz et al. [24]. Owing to

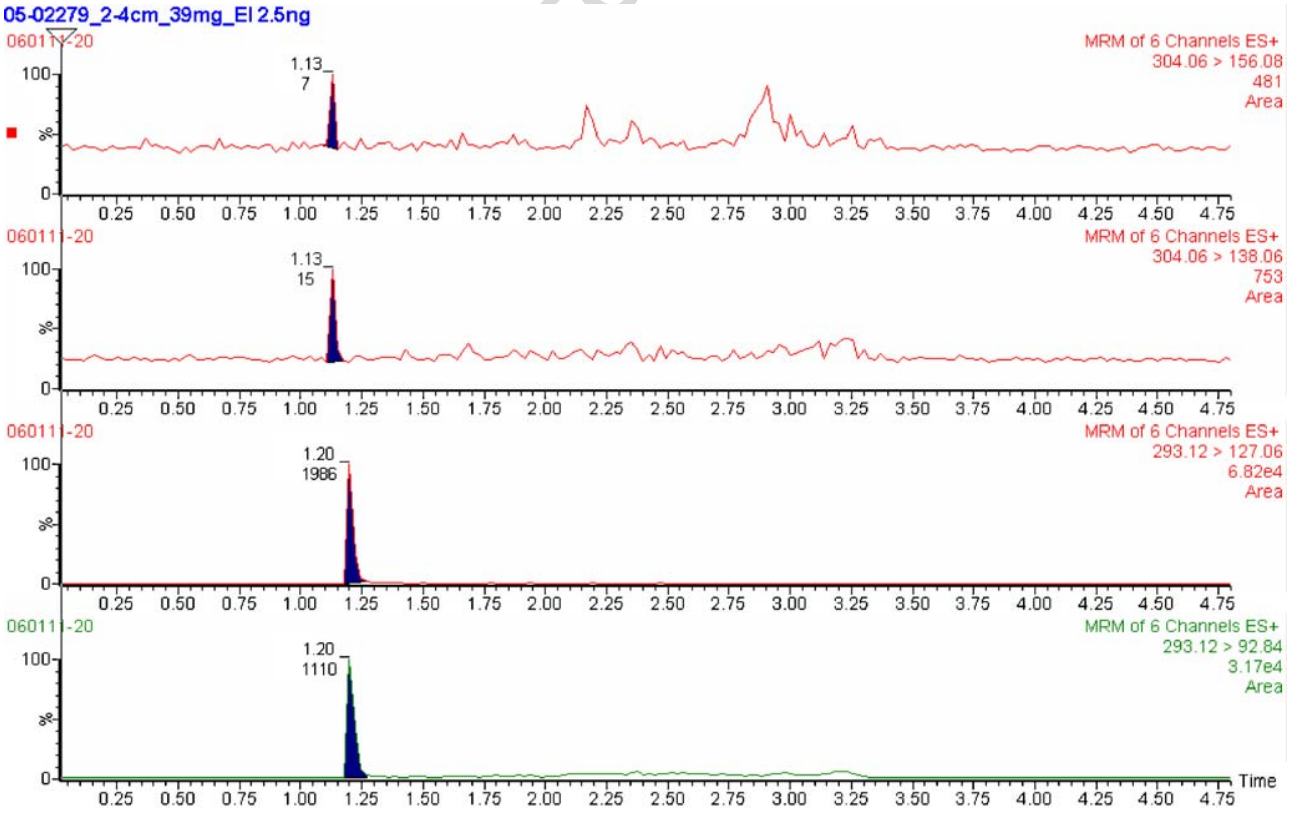

Fig. 2 Chromatogram of a hair extract from the second segment (2–4 cm) from subject 2. Scopolamine concentration was 0.3 pg/mg. *From the top to the bottom*: the two product ions of scopolamine and the two product ions of atropine-d_3

the long delay between the alleged crime and clinical examination, collection of blood or urine was of little value. This is the reason why the laboratory developed an original approach based on hair testing by LC-MS/MS. A strand of hair from each child was sampled about 2 months after the first suspicion of administration and was cut into small segments. After being cut into small pieces, 20 mg of hair was incubated overnight in a phosphate buffer (pH 8.4). The aqueous phase was extracted by a mixture of diethyl ether/dichloromethane (80:20), in the presence of diazepam-d_5, used as an internal standard. Hair extract was separated on an XTerra MS C18 column using a gradient of acetonitrile and formate buffer. Detection was based on two daughter ions: transitions m/z 299.3 to 299.0 and 100.0 and m/z 289.9 to 154.0 for trimeprazine and the internal standard, respectively. In the hair of the two subjects, trimeprazine was detected at concentrations in the range 23–339 pg/mg. The mother-in-law, who was the perpetrator in both cases, did not challenge the use of trimeprazine as a sedative drug.

Diphenhydramine

Diphenhydramine was one of the first effective antihistamine agents to have been discovered. The compound is also used for its sedative and antiemetic effects. The first case involving repetitive sedation linked to the use of diphenhydramine as a DFC and subsequent impairment of a 9-year-old female victim was reported by Kintz et al. [25]. Owing to the long delay between the alleged crime and clinical examination, collection of blood or urine was of little value; hence, the laboratory developed an original approach based on hair testing by LC-MS/MS. A single strand of hair from the victim was sampled about 7 weeks after the last suspected administration and was cut into

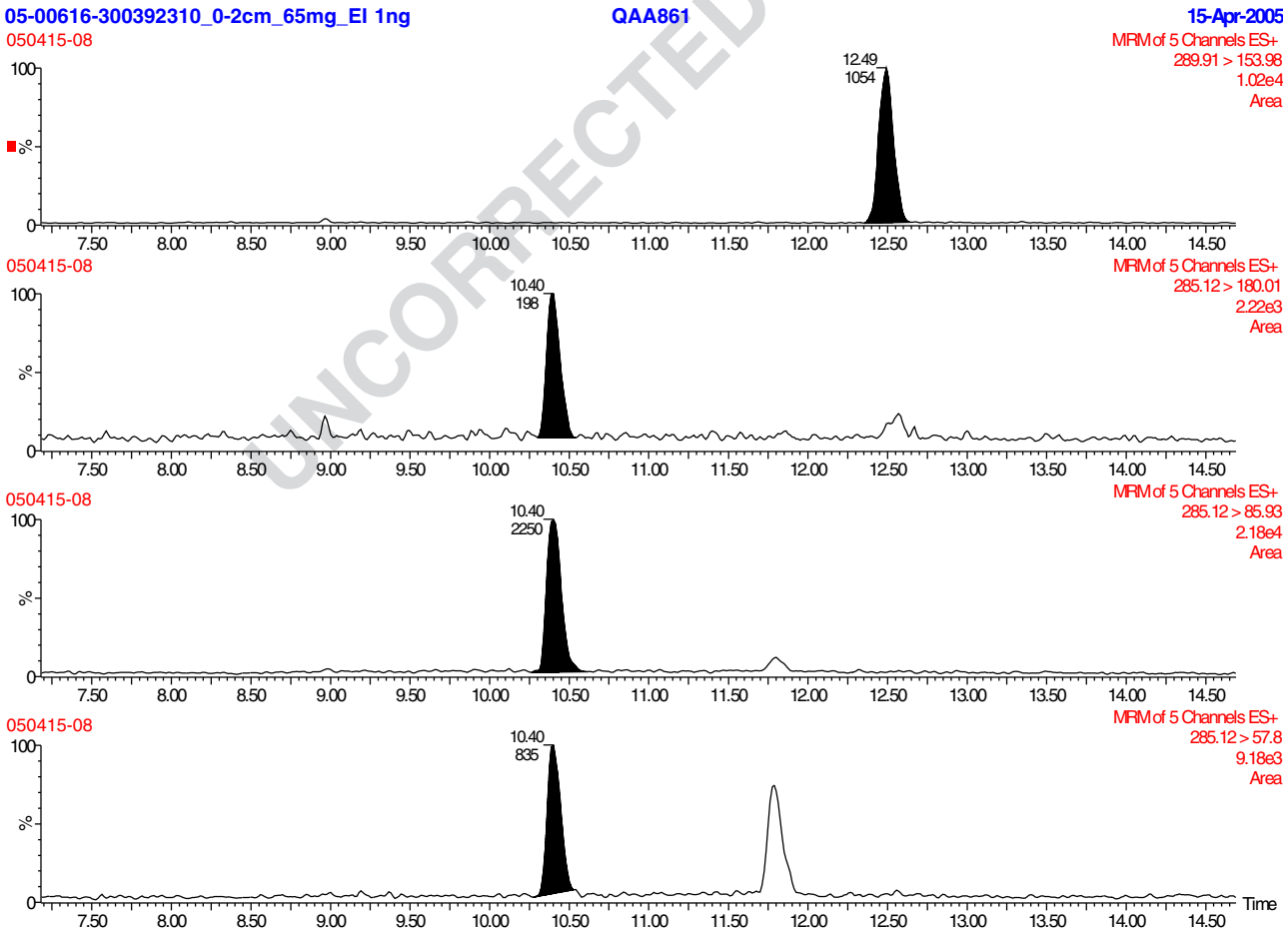

Fig. 3 Liquid chromatography–tandem mass spectrometry chromatogram of a white hair extract (segment root to 2 cm) obtained from an elderly person sedated with promazine. The drug concentration was 9 pg/mg. *From the top to the bottom*: Product ion of the internal standard and the three product ions of promazin

small segments. After being cut cut into small pieces, about 20 mg of hair per segment was incubated overnight in a phosphate buffer (pH 8.4). The aqueous phase was extracted with 5 ml of a mixture of dichloromethane/diethyl ether (80:20), in the presence of diazepam-d_5, used as an internal standard. The hair extract was separated on an XTerra MS C18 column using a gradient of acetonitrile and formate buffer. Detection was based on two daughter ions: transitions *m/z* 256.2 to 152.1 and 167.1 and *m/z* 289.9 to 154.0 for diphenhydramine and the internal standard, respectively. In the hair of the child, diphenhydramine was detected at concentrations in the range 33–39 pg/mg, depending on the segment.

Promazine

In a review devoted to the role of hair in drug detection, Kintz et al. [26] reported the case of an elderly person sedated with promazine. The drug was identified using the same procedure as for benzodiazepines [10] by LC-MS/MS. Despite the white hair of the subject, it was possible to detect promazine at 9 pg/mg. Figure 3 represents the chromatogram of the hair extract.

Discussion

From literature data, it is obvious that the target concentrations in hair after a single exposure are in the range of few picograms/milligrams. To obtain the required ultralow limits of detection together with suitable MS information, MS/MS appears to be a prerequisite. Selectivity and sensitivity are extraordinarily increased by almost completely suppressing the noise level. In comparison with the concentrations that are measured with drugs of abuse, such as heroin or cocaine, in case of DFC, the concentrations are at least 1,000 times lower.

As is the case with other applications (survey of addicts, doping control, reissuing of driving license), hair testing is a valuable approach to increase the window of drug detection. Embarrassment associated with urine collection, particularly after sexual assault, can be greatly mitigated through hair analysis. It is always possible to obtain a fresh, identical hair sample if there is any trouble during analysis, claim of specimen mix-up or breach in the chain of custody. This makes hair analysis essentially fail-safe, in contrast to blood or urine analysis, since an identical blood or urine specimen cannot be obtained at a later date. The discrimination between a single exposure and long-term use can be documented by multisectional analysis. With the concept of absence of migration along the hair shaft, a single spot of exposure must be present in the segment corresponding to the period of the alleged event, using a growth rate for hair of 1 cm/month. As this growth rate can vary from 0.7 to 1.4 cm/month, the length of the hair section must be calculated accordingly. A delay of 4–5 weeks between the offense and hair collection and sectional analysis of 2-cm sections was considered as satisfactory to have the hair shaft including the spot of exposure. The hair must be cut as close as possible to the scalp. Particular care is also required to ensure that the individual hair in the strand retains the position it originally had beside the other hairs. Cheze et al. [27] have confirmed in more than 100 cases the value of sectional analyses. In their series, the prevalence of zolpidem and clonazepam was high.

The unique possibility to demonstrate a single drug exposure through hair analysis has some additional interest. In the case of late crime declaration, positive hair findings are of paramount importance for a victim, in order to start under suitable conditions a psychological follow-up. It can also help in the discrimination of a false report of assault, for example, in the case of revenge. These cases are often sensitive with little other forensic evidence. Tedious interpretations, in the case of concomitant intake of hypnotics as a therapy for sleeping disorders, are avoided when investigations are done using hair in addition to urine.

Some authors in general reviews on the applications of hair have demonstrated that this approach has several indications in the case of DFC [28–30], confirming our previous investigations.

Conclusion

It appears that the value of hair analysis for the identification of DFC is steadily gaining recognition. At this time, about six laboratories in France are able to test for these drugs in hair. Hair analysis may be useful adjunct to conventional drug testing, using blood and urine. Specimens can be more easily obtained with less embarrassment, and hair can provide a retrospective tool to demonstrate drug exposure.

Although there are still controversies on how to interpret the results, particularly concerning external contamination, cosmetic treatments, ethnical bias or drug incorporation, pure analytical work in hair analysis has reached a sort of plateau, having solved almost all the analytical problems.

Although GC-MS is the method of choice in practice to test for drugs of abuse, GC-MS/MS or LC-MS/MS are today used for routine cases, particularly to target drugs with low concentrations. In the case of DFC, hair testing should be used to complement conventional blood and urine analysis as it increases the window of detection and permits differentiation, by segmentation, of long-term therapeutic use from a single exposure. Selectivity and sensitivity of MS/MS are a prerequisite in DFC cases.

References

1. Wells D (2001) Sci Justice 41:197–199
2. Hindmarch I, ElSohly M, Gambles J et al (2001) J Clin Forensic Med 8:197–205
3. LeBeau M, Andollo W, Hearn WL et al (1999) J Forensic Sci 44:227–230
4. Kintz P, Cirimele V, Goullé JP, Ludes B (2001) Clin Chem 47:2033–2034
5. Verstraete A (2002) Ann Toxicol Anal 14:390–394
6. Goullé JP, Chèze M, Pépin G (2003) J Anal Toxicol 27:574–580
7. Kintz P, Cirimele V, Jamey C, Ludes B (2003) J Forensic Sci 48:195–200
8. Shen M, Liu XQ, Liu W, Xiang P, Shen B (2006) Fa Xi Xue Za Zhi 22:48–51
9. Laloup M, Ramirez Fernandez M, De Boeck G, Wood M, Maes V, Samyn N (2005) J Anal Toxicol 29:616–626
10. Villain M, Concheiro M, Cirimele V, Kintz P (2005) J Chromatogr B 825:72–78
11. Villain M, Chèze M, Dumestre V, Ludes B, Kintz P (2004) J Anal Toxicol 28:516–519
12. Kintz P, Villain M, Dumestre-Toulet V, Ludes B (2005) J Clin Forensic Med 12:36–41
13. Villain M, Chèze M, Tracqui A, Ludes B, Kintz P (2004) Forensic Sci Int 143:157–161
14. Villain M, Chèze M, Ludes B, Kintz P (2004) Forensic Sci Int 145:117–121
15. Kintz P, Villain M, Chèze M, Pépin G (2005) Forensic Sci Int 153:222–226
16. Kintz P, Villain M, Cirimèle V, Pépin G, Ludes B (2004) Forensic Sci Int 145:131–135
17. Chèze M, Villain M, Pépin G (2004) Forensic Sci Int 145:123–130
18. Frison G, Favretto D, Tedeschi L, Ferrara SD (2003) Forensic Sci Int 133:171–174
19. Villain M, Tournoud C, Flesch F, Cirimele V, Kintz P (2006) J Chromatogr B 842:111–115
20. Bartsch C, Risse M, Schütz H, Weigand N, Weiler G (2003) Forensic Sci Int 137:147–151
21. Sporkert F, Augsburger M, Brandt-Casadevall C, Mangin P (2005) Ann Toxicol Anal 17:127
22. Pépin G, Chèze M, Duffort G, Vayssette F (2002) Ann Toxicol Anal 14:395–406
23. Kintz P, Villain M, Pujol ML, Salquebre G, Cirimele V (2006) In: Society of Forensic Toxicologists annual meeting, Austin
24. Kintz P, Villain M, Cirimele V (2006) J Anal Toxicol 30:400–402
25. Kintz P, Evans J, Villain M, Cirimele V (2007) Forensic Sci Int (in press)
26. Kintz P, Villain M, Cirimele V (2006) Ther Drug Monit 28:442–446
27. Cheze M, Duffort G, Deveaux M, Pépin G (2005) Forensic Sci Int 153:3–10
28. Negrusz A, Gaensslen RE (2003) Anal Bioanal Chem 376:1192–1197
29. Saint-Martin P, Furet Y, O'Byrne P, Bouyssy M, Paintaud G, Autret-Leca E (2006) Thérapie 61:145–150
30. Pragst F, Balikova MA (2006) Clin Chim Acta 370:17–49

Springer

AUTHOR QUERY FORM

Dear Author,

During the preparation of your manuscript for typesetting, some questions have arisen. These are listed below. Please check your typeset proof carefully and mark any corrections in the margin of the proof or compile them as a separate list.

Queries and/or remarks

Location in Article	Query / remark
	No query.

Thank you for your assistance