Fatal Case of a 27-Year-Old Male After Taking Iboga in Withdrawal Treatment: GC-MS/MS Determination of Ibogaine and Ibogamine in Iboga Roots and Postmortem Biological Material

6 authors, including:

Cédric Mazoyer
http://www.cedric-mazoyer.fr
11 PUBLICATIONS **54** CITATIONS

SEE PROFILE

Jeremy Carlier
Sapienza University of Rome
33 PUBLICATIONS **222** CITATIONS

SEE PROFILE

Alexandra Boucher
Saint Catherine University
8 PUBLICATIONS **35** CITATIONS

SEE PROFILE

Michel Péoc'h
Centre Hospitalier Universitaire de Saint-Étienne
284 PUBLICATIONS **3,253** CITATIONS

SEE PROFILE

Some of the authors of this publication are also working on these related projects:

Anterolateral ligament: research View project

NPS metabolism View project

CASE REPORT

TOXICOLOGY

Cédric Mazoyer,[1] M.Sc.; Jérémy Carlier,[1] M.Sc.; Alexandra Boucher,[2] Pharm.D.; Michel Péoc'h,[3] M.D., Ph.D.; Catherine Lemeur,[4] Pharm.D.; and Yvan Gaillard,[1] Pharm.D., Ph.D.

Fatal Case of a 27-Year-Old Male After Taking Iboga in Withdrawal Treatment: GC-MS/MS Determination of Ibogaine and Ibogamine in Iboga Roots and Postmortem Biological Material*

ABSTRACT: We report the case of a man who died twelve hours after ingesting powdered iboga root, commonly taken for its stimulant and hallucinogenic properties. Ibogaine and ibogamine were quantified in the powder ingested and the victim's body fluids by GC-MS/MS after liquid–liquid extraction (Toxi-tubes A®). The concentrations of ibogaine measured in the blood samples taken at the scene and in the peripheral blood, urine, and gastric fluid samples taken during the autopsy were 0.65, 1.27, 1.7, and 53.5 μg/mL, while the iboga content in the powder was 7.2%. Moreover, systematic toxicological analyses of biological samples showed the presence of diazepam and methadone in therapeutic concentrations. Death was attributed to the ingestion of a substantial quantity of iboga in the context of simultaneous methadone and diazepam consumption.

KEYWORDS: forensic science, forensic toxicology, *Tabernanthe iboga*, ibogaine, ibogamine, gas chromatography–tandem mass spectrometry, poisoning

Tabernanthe iboga, usually called *iboga* or *eboka*, is an angiosperm shrub of the Apocynaceae family that grows wild in some tropical African forests, particularly in Gabon, but also in the Republic of Congo, Cameroon, and Guinea (1–3). The plant grows to a height of 1.5–2 m and grows small yellow, pink, or speckled white flowers and orange fruit with sweet-tasting flesh (Fig. 1) (2). Its yellowish roots contain a dozen psychotropic indole alkaloids (their bark contains 5–6 percent of these), the most important being ibogaine, and they are commonly taken in traditional magico-religious rituals in some indigenous communities (1–3). Iboga root can be taken fresh, but is generally dried. It is ingested in thin strips or grated into a powder, on its own or mixed with palm wine or water (2,3).

Taken in small doses (<50 mg of ibogaine), it has stimulant, anorexigenic, and euphoriant, even aphrodisiac effects (1,3). Its use as a stimulant by Congolese hunters has been recorded since the 19th century (2,3). A medicine based on a weak concentration of total extracts of *Tabernanthe* iboga, LAMBARENE®, was on the market in France from 1939 to 1968. It was recommended for asthenia, physical, intellectual, or psychological depression, convalescence, overwork, age-related or pathological disabilities, although it was widely used as a doping substance by mountaineers, cyclists, and long-distance runners until 1966 (4,5).

Moderate doses (from 100 mg to 1 g of ibogaine) cause trance-like visual and auditory hallucinations, altered time perception, and auditory, olfactory, and gustatory synesthesia as well as diarrhea and vomiting (1–3). Iboga is rarely taken as a recreational or psychedelic drug. It is used above all as an entheogen in certain African tribes, particularly in the *Bwiti* cult in Gabon. In Bwiti, which was inherited from the pygmies, the *banzi* (initiate) ingests massive doses of iboga during complex initiation rites in the presence of the tribe and the *nganga* (the community's chief spiritual healer) and accompanied by music and dancing. Taking iboga root is in this case a way of making contact with the ancestors in the "spirit world" and of "reconciling oneself with death" (2,3). Although it is an ancient religion, the numbers of followers of Bwiti have grown in recent years. It forms a bulwark against the modern foreign cultures that are establishing themselves in a society undergoing

[1]Laboratoire LAT LUMTOX, 800 av. Marie Curie, Z.I. Jean Jaurès, 07800 La Voulte-sur-Rhône, France.
[2]Centre d'Evaluation et d'Information sur la Pharmacodépendance de Lyon, 162 av. Lacassagne, 69424 Lyon, France.
[3]Service de Médecine Légale, Hôpital Bellevue, 25 bvd. Pasteur, 42055 Saint-Etienne, France.
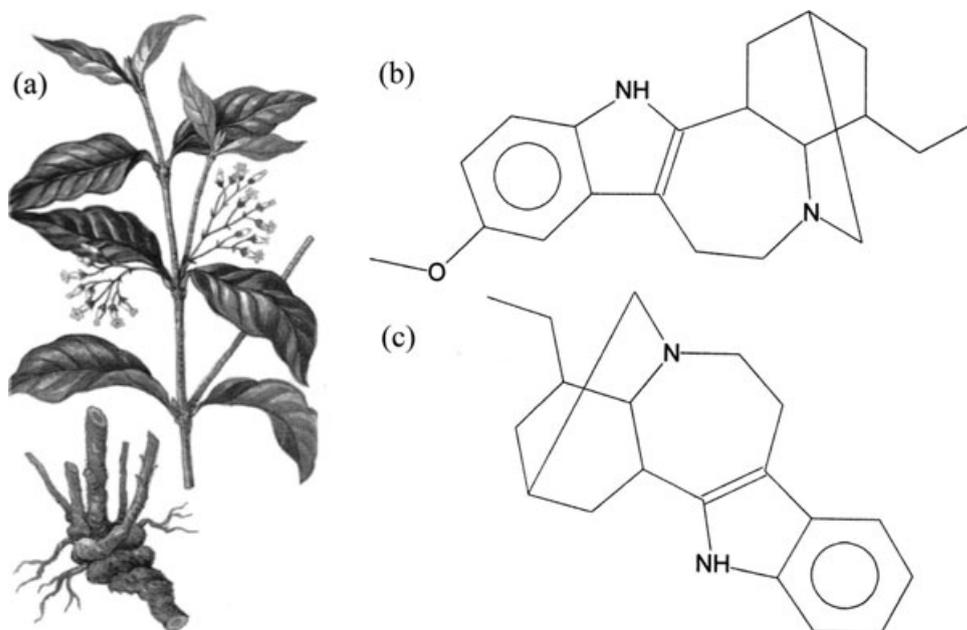[4]Laboratoire LAT LUMTOX, 71 av. Rockefeller, 69003 Lyon, France.

FIG. 1—*Representation of the structures of ibogaine (b) and ibogamine (c), indole alkaloids present in the root bark of Tabernanthe iboga, an angiosperm shrub of the Apocynaceae family (a).*

major changes and particularly against the Christianity of Europe and Islam of the Middle East (2,3). In the West, ibogaine has been used for therapeutic reasons since 1969, when the Chilean psychotherapist Claudio Naranjo used it as a catalyst in the therapeutic process. He described the substance as an inducer of dreams without loss of consciousness (1,5). From the 1980s onwards, Howard Lotsof maintained that "this substance can be a simple and effective medicinal means to cure almost all addictions" and applied for several patents for the use of ibogaine to treat chemical dependence on opiates, stimulants (cocaine and amphetamine), alcohol, and nicotine. There were many studies of the anti-addictive effect of ibogaine on animals in the 1990s, but most of the data on humans come from informal reports by patients' associations. There are as yet no real clinical trials supported by a proven methodology, yet the number of institutions offering ibogaine treatments is growing (1,5).

Strong doses of iboga lead to epileptic manifestations, fainting, paralysis, hypothermia, respiratory failure, and can be lethal. To date, eighteen deaths linked with ibogaine ingestion have been recorded (1,5–11). In the late 1960s, the World Health Assembly classified ibogaine with hallucinogens and stimulants as a substance likely to cause dependency or endanger human health (1). The consumption of iboga, ibogaine, and their analogs is forbidden in France by the decree of March 12, 2007, confirmed by the Council of State, March 20, 2009.

The most abundant alkaloid present in the roots of the shrub is ibogaine or 12-methoxyibogamine (~ 80 percent); there are weaker concentrations of tabernanthine, ibogaine, and ibogamine (~ 5 percent) (Fig. 1) (2,3,6). The effects and toxicity of ibogaine seem to be related to its simultaneous action on a group of neurotransmitter systems in the autonomous central nervous system and appear not to be attributable to actions at any single type of receptor, while its mechanism is complex and still only partially understood (1,3,9). Ibogaine has been the subject of several different methods of identification and analysis using chromatographic techniques combined with mass spectrometry/gas chromatography combined with mass spectrometry (GC-MS)

in body fluids in the 1990s (12–15), then high-performance liquid chromatography combined with mass spectrometry (HPLC-MS) in blood (16), and more recently HPLC combined with tandem mass spectrometry (HPLC-MS/MS) in body fluids (10,17).

In this article, we report a fatal case of ibogaine poisoning through the ingestion of powdered root bark of *Tabernanthe iboga*. Quantification of ibogaine and ibogamine in the postmortem samples was carried out by an original method of GC combined with a tandem mass spectrometer (GC-MS/MS) after liquid–liquid extraction (LLE).

Case Report

The victim, a 27-year-old Caucasian man (1.77 m tall and weighing 67 kg), was found dead around 11.00 am in 2006 in Ardèche, France, during a detoxification program organized by a group that specialized in seminars on personal development and the discovery of iboga. The people in charge of the group, who were present at the time of death, claimed that the victim had ingested "a teaspoon" of powdered iboga root on the night before. The victim had been addicted to various substances for roughly 15 years: alcohol, cannabis (resin and herbal), psilocybin, benzodiazepines (diazepam, nordiazepam, flunitrazepam), cocaine and crack, amphetamine, ecstasy, LSD, morphine, and heroin by his own admission. He had been undergoing a methadone-based substitution treatment for 4 years (lately 30 mg a day) at the time and had taken his last dose two nights prior to his death; he had also been taking a diazepam (VALIUM®) treatment for ten years (lately 50 mg a day).

The autopsy was unable to establish any traumatic origin for the death of the victim, whereas the anatomo-pathological examination of the heart–lung block showed the presence of exogenous elements in the pulmonary parenchyma and various calibers of bronchial tubes, indicating that regurgitation had taken place that was substantial and extensive enough to have caused asphyxiation (Mendelson's syndrome). No underlying cardiac or pulmonary pathology was detected.

A sample of blood (subclavian vein) was taken at the scene of death 7 h after the declaration of death, and samples of peripheral blood (femoral artery), urine, and gastric fluid were taken during the autopsy 8 days later. The rest of the powder consumed was also analyzed. Specimens were stored at +4°C until analyses were carried out 2 weeks later.

Materials and Methods

Chemicals and Reagents

Ibogaine, ibogamine, and prazepam-d5 standards were purchased from LGC Standards (Molsheim, France), Toxi-tubes A® from Varian (Courtaboeuf, France). Purified water was provided by VWR® (Fontenay-sous-Bois, France), while methanol and ethyl acetate for HPLC were provided by Sigma-Aldrich® (Saint-Quentin Fallavier, France).

The stock solution of ibogaine, ibogamine, and their dilutions in methanol were stored at +4°C and protected from light. Prazepam-d5 was used as an internal standard (IS).

Extraction Procedure

Body fluids were extracted by means of Toxi-tubes A®. 20 μL of prazepam-d5 (10 μg/mL, 200 ng) and 500 μL of blood or urine, or 50 μL of gastric juice was added to the Toxi-tubes and topped up with 5 mL of deionized water then mixed by gentle inversion for 10 min. After centrifugation for 10 min at 3000 g, the organic supernatant was evaporated under a stream of air at +50°C. The residue was then reconstituted by 50 μL of ethyl acetate and transferred into a vial for injection into the gas chromatographic system.

Quantification ranges in body fluids were carried out on six calibration levels plus a blank at 10, 50, 100, 500, 1000, and 2000 ng/mL of ibogaine and ibogamine. Drug-free material previously tested negative for the targeted molecules was taken from different autopsied corpses.

About 100 mg of the powder was sonicated for 20 min in 1 mL of methanol together with 10 μL of prazepam-d5. After centrifugation for 10 min at 3000 g, 50 μL of the solution was evaporated to dryness under a stream of air at +50°C. The residue was then reconstituted by 50 μL of ethyl acetate and transferred into a vial for injection into the gas chromatographic system.

Calibration was performed in powdered local dried roots of *Verbascum thapsus* (morphological similarities) previously tested negative for ibogaine and ibogamine by our method.

GC-MS/MS Procedure

The gas chromatography used was a Trace GC (Thermo Scientific, Courtaboeuf, France) equipped with an AS3000 autoinjector and a PolarisQ mass spectrometer (electron ionization).

The analytical column was a FactorFour™ capillary column 5% phenyl, 95% methyl siloxane, 30 m in length, with an internal diameter of 0.25 mm (0.50 μm film thickness) from Varian (Courtaboeuf, France). Helium (6.0 purity) was used as carrier gas at a flow rate of 1 mL/min in constant flow mode. The interface temperature was +280°C, and ion source temperature was +200°C. Pulsed injection with surge pressure (1 μL) was carried out at +280°C and 200 kPa for 1 min. The initial oven temperature was +50°C for 2 min and was increased to +300°C at 25°C/min and held for 8 min. The chromatographic analysis lasted 20 min.

The measurements were made in selected reaction monitoring mode (SRM). For ibogaine and ibogamine, the pseudomolecular ions were isolated (m/z = 310 and 280, respectively) and quantified by majority transition (m/z = 225 and 195, respectively). The identifications were confirmed by the full spectra (full-scan spectra and full-scan product ion spectra) (Fig. 2).

Systematic Toxicological Analyses (STA)

STA procedures include headspace gas chromatography–mass spectrometry (GC-MS) for the analysis of ethanol and other volatile substances, GC-MS after acetylation with the use of CARIBOU® software (personal communication), high-performance liquid chromatography photodiode array detection (HPLC-PDA) (18), UPLC-PDA/MS (personal communication) as well as immunoassay techniques, carbon monoxide, and cyanide detection.

Results

The calibration curves obtained for ibogaine were linear for concentrations from 10 to 2000 ng/mL in the body fluids and from 1 to 100 μg/mg in the powder, with correlation coefficients >0.999. The detection limit was calculated from the mathematical formula LOD = m_{bl} + 3SD_{bl} (m_{bl}: mean of the blanks; SD_{bl}: standard deviation of the blanks; n = 30) as 1 ng/mL for the two analytes in the blood and urine, while it was 20 ng/mL in the gastric fluid. Within- and between-day precision studies gave relative standard deviations (RSD) always <12% in the whole calibration range in blood and urine.

The concentrations of ibogaine and ibogamine measured in the victim's blood were positive at 650 and 50 ng/mL, respectively, in the subclavian blood sample taken at the scene of death and 1270 and 100 ng/mL, respectively, in the femoral blood sample taken at the autopsy. The concentrations measured in the urine and gastric fluid samples during the autopsy were also positive for ibogaine (1700 and 53,500 ng/mL, respectively) and ibogamine (120 and 4340 ng/mL, respectively) (Table 1, Fig. 3).

The results of STA are shown in Table 1.

The powder ingested by the victim contained 7.2 percent ibogaine and 0.6 percent ibogamine. A teaspoonful of 1.5–2 g of the powder contains approximately 108–144 mg of ibogaine and 9 to 12 mg of ibogamine.

Discussion

Toxicological tests identified the presence of significant quantities of ibogaine and ibogamine in all the biological samples taken from the victim at the scene of death and during the autopsy. These results confirm that the individual had consumed iboga root.

The ibogaine and ibogamine contents found in the powder (7.2 and 0.6 percent, respectively) are comparable to those found in extracts of powdered *Tabernanthe iboga* root and to the pharmacognostic data reported in the literature (1–3,6). No other toxic compound, foreign to the plant, was detected by complementary analyses. Bogusz et al. showed that a dose of 20 mg/kg, or the ingestion of 1400 mg of ibogaine, would result in an ibogaine concentration of 150 ng/mL in a man weighing 70 kg (the approximate weight of our victim) 19 h after ingestion (7). In that case, the concentrations measured in the victim would be the result of ingesting larger quantities than the
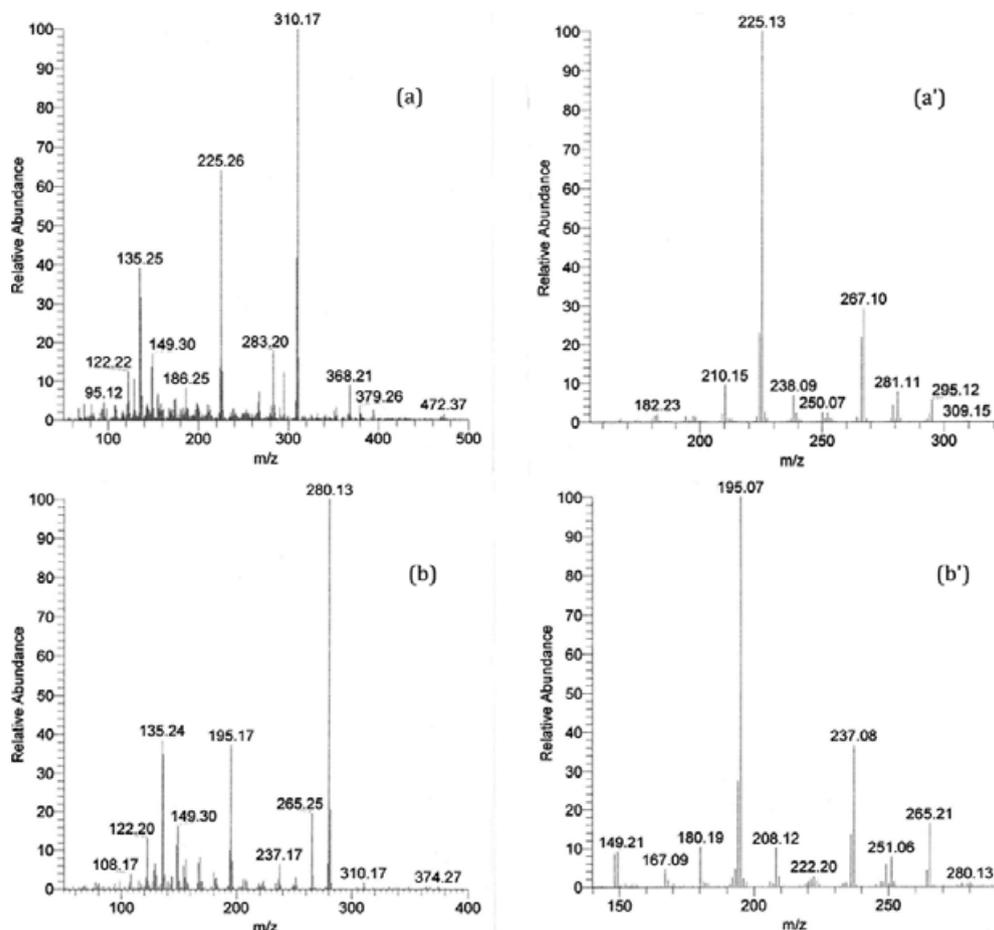
FIG. 2—*Full-scan mass spectra of ibogaine (a) and ibogamine (b). Full-scan production spectra obtained from pseudomolecular ion of ibogaine (m/z = 310) (a') and ibogamine (m/z = 280) (b').*

TABLE 1—*Concentrations of the different compounds analyzed, as measured in the victim's postmortem samples (ng/mL or ng/g). The quantities measured in the gastric contents are given as the total mass recovered from the gastric contents (μg in brackets).*

Compound	Blood (scene: subclavian vein)	Peripheral Blood (autopsy: femoral artery)	Urine (autopsy)	Gastric Juice (autopsy)
Ibogaine	650	1270	1700	53,500 (2675)
Ibogamine	50	100	120	4340 (217)
Diazepam	413	175	35	786 (39.3)
Nordiazepam	350	173	60	650 (32.5)
Oxazepam	90	10	40	ND
Temazepam	40	20	30	ND
Methadone	77	74	175	3 (0.15)
EDDP	20	21	1300	98 (4.9)

ND, not detected.

teaspoonful that had been alleged by the group; it could easily have been a dose of over 20 g of the iboga powder analyzed.

To date, at least eighteen cases of fatal ibogaine poisoning have been reported in psychotherapeutic settings or with anti-addictive aims, but cases in which the concentrations of the active principles have been established in postmortem samples are rare (1,5–11). In 1998, Bogusz et al. reported a fatal case of iboga poisoning that had occurred in June 1993 in the Netherlands. The 24-year-old victim had ingested a 29 mg/kg dose of ibogaine as part of a heroin addiction treatment and died of respiratory failure 19 h later. The concentration of ibogaine measured in the femoral blood was 710 ng/mL, and the victim was suspected of secretly taking opiates during the treatment (7). In 2006, Kontrimavičiūtė et al. reported the case of a 48-year-old man with a history of drug addiction who died 53 h after taking iboga. The concentration of ibogaine measured in a sub-clavian blood sample taken at the scene of death, between 6 and 12 h after death, was 10,800 ng/mL; the concentrations from samples of femoral blood, urine, and gastric contents taken during the autopsy 48 h later were 5400, 83,300, and 2910 ng/mL, respectively (6). To date, there is no conclusive explanation for the cause of these deaths. Some authors implicate that the cerebellar neurotoxicity produced by ibogaine observed mainly in rats (1,8), others suspect a deregulation of the autonomic nervous system combined with psychological stress, causing sudden cardiac arrest, the risk of which would be greater if there were a pre-existing cardiac anomaly (9,10,19). In 2009, Hoelen et al. reported the case of a woman admitted to hospital as an emergency after having a heart attack brought about by the consumption of a single moderate dose of around 500 mg of ibogaine. The patient presented with extreme severe QT interval prolongation (548 ms; QT interval corrected for the heart rate (QTc), 616 ms) and ventricular tachyarrhythmias. QT interval prolongation is a risk factor for torsades de pointes and ventricular fibrillation, which can lead to sudden death. The authors proposed a
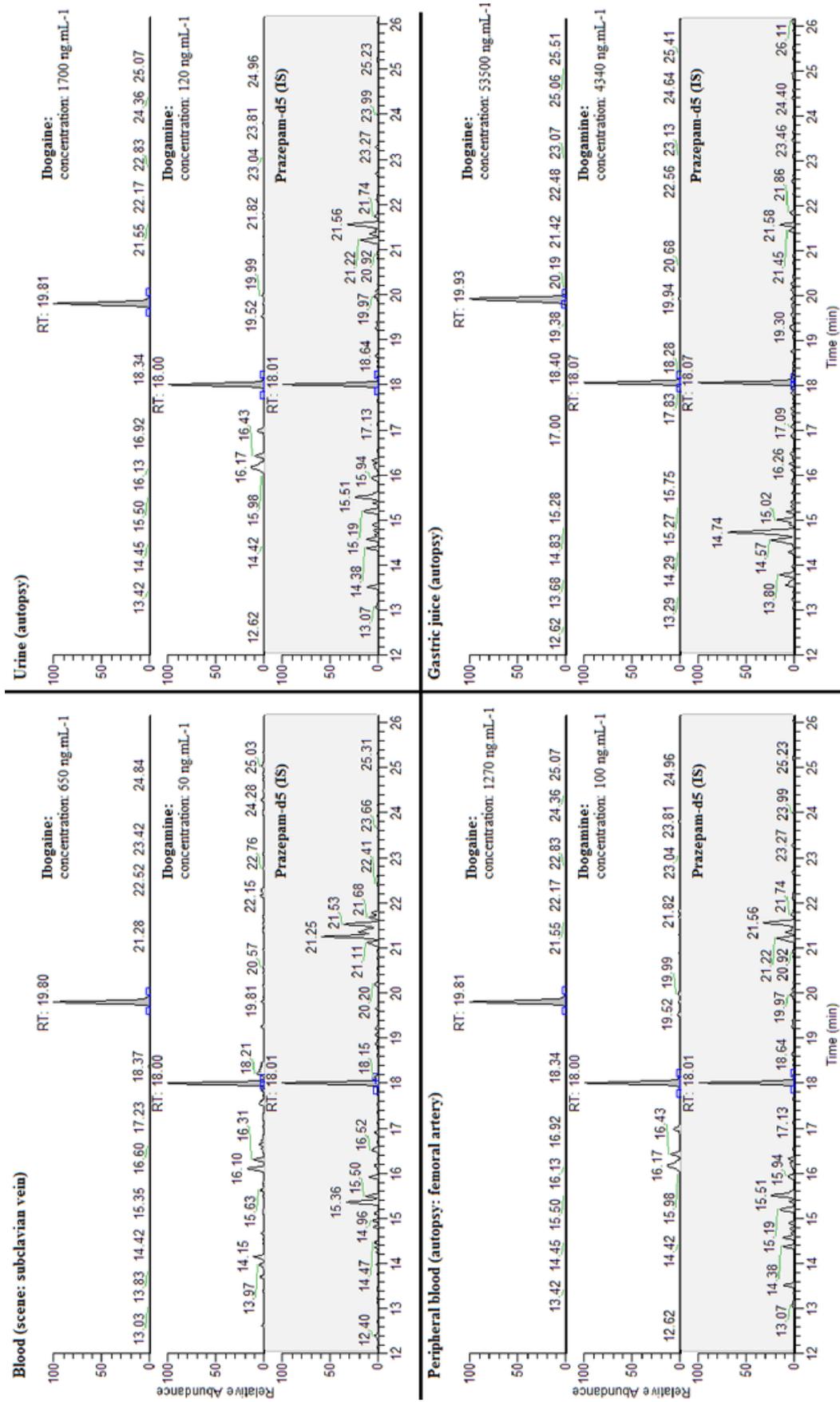
FIG. 3—*Chromatograms of the victim's postmortem biological samples (IS: internal standard; RT: retention time).*

cause of death associated with the consumption of ibogaine in the occurrence of QT interval prolongation and ventricular tachyarrhythmias (19). In addition, there are some indications suggesting that taking ibogaine and opiates simultaneously increases the toxicity of the opiates (1,6,7,11).

The STA indicated the presence of methadone and its inactive metabolite in the victim's samples. The concentrations of methadone measured in the blood were therapeutic for an inexperienced individual, or infratherapeutic for a long-term user like the victim, and consistent with having last been taken 48 h before death, as alleged by witnesses (20). Methadone is known to cause QT interval prolongation and fatal torsades de pointes, hence the publication of security recommendations for doctors in 2009 (21,22). In particular, it is recommended not to exceed a QT interval of 500 ms and not to prescribe methadone together with other substances that prolong the interval.

The presence in the samples of therapeutic concentrations of diazepam and its active metabolites (nordiazepam, oxazepam and temazepam) confirms that the victim, who was taking a VALIUM® treatment, had consumed diazepam. Bearing in mind his drug-addicted past (dipotassium clorazepate abuse), coconsumption cannot be ruled out. The quantification of these compounds in the urine was not very informative: the relative ratios of the metabolites of diazepam in urine are variable and dose dependent, and their absolute concentration clearly depends on the individual's diuresis (20). Reports of methadone-related deaths often mention the simultaneous consumption of benzodiazepines (23). A mechanism of action was proposed recently that explained the potentialization of the harmful cardiac effects of methadone by diazepam (24).

As there is so little information available on postmortem concentrations of ibogaine after the ingestion of iboga root, it is difficult to come to any firm conclusions about the cause of death. However, our analyses seem to be consistent with the results already published. Hoelen et al. reported the case of QT interval prolongation in a woman who had taken a moderate dose of iboga. Our victim had taken roughly three times the amount, together with methadone, which is known to prolong the QT interval, and diazepam, known to potentialize the cardiotoxicity of methadone. The consumption of a substantial amount of iboga appears thus to be the cause of death, in the context of simultaneous diazepam and methadone consumption. Moreover, concentrations of diazepam, methadone, and their metabolites are insufficient to account for death in a context of regular consumption over several years. In this hypothesis, sudden cardiac death resulted from torsades de pointes caused by QT interval prolongation.

It is interesting to note that the concentrations of ibogaine and ibogamine measured in the blood sampled during the autopsy are twice as high as those in the blood sampled at the scene of death. This contradicts the data previously reported by Kontrimavičiūtė et al., who measured concentrations in the subclavian blood sampled at the scene of death that were twice as high as those measured in the femoral blood sampled during the autopsy 48 h later (6). The hypothesis of postmortem degradation of ibogaine proposed by the authors is not necessarily disproved in our case, but the degradation could be offset by substantial postmortem redistribution (PMR) of the two compounds, which could make the interpretation of the analyses more complicated. The main sources of PMR are the liver, the gastric and digestive contents, and the lungs. Xenobiotics in the liver and lungs spread out gradually by passive diffusion,

mainly into the cardiac cavities and large thoracic vessels, while redistribution into the peripheral system appears to be a more moderate and slower process. The passive absorption of xenobiotics from the gastric and digestive contents into the mesenteric blood can take place after death, as long as there is a concentration gradient, so they can diffuse gradually into the adjacent organs (25). In our case, the concentrations of ibogaine (volume of distribution (Vd) approximately 5 L/kg (26)) and ibogamine measured in the victim's gastric contents were very substantial compared with the other samples. If degradation of the two molecules had occurred between the two blood samples, the difference may have been offset by diffusion of the gastric and digestive contents into nearby organs, including the femoral artery. In addition, the samples were taken from different sites (subclavian vein and femoral artery) and at different postmortem intervals (7 h and 8 days, respectively). The subclavian vein is a questionable choice of site for a peripheral blood sample because of its proximity to the heart (27). Indeed, benzodiazepines are often found in higher concentrations in cardiac blood than those in peripheral blood (28) and do not seem to be very prone to postmortem degradation. The concentrations of diazepam (Vd, 0.5–2.5 L/kg (20)), nordiazepam (Vd, 0.5–2.5 L/kg (20)), oxazepam (Vd, 0.5–2 L/kg (20)), and temazepam (Vd, approximately 1 L/kg (20)) measured in the victim are therefore consistent with early PMR (within 7 h of death). According to this hypothesis, the ibogaine concentrations measured by Kontrimavičiūtė et al. were more likely to be the result of PMR than of degradation. Moreover, the concentrations measured in our victim would have been overestimated. The concentrations of methadone (Vd, 4–5 L/kg (20)) and EDDP were same in both samples, which may show that they have a slower rate of PMR.

The legal proceedings against the people in charge of the group who organized the detoxification treatment are still ongoing. The forensic scientist concluded that the death was a direct result of taking iboga. Iboga, ibogaine, and their analogs have been classified as controlled substances in France since March 2007; the decree came as a direct result of the death of our victim and another case in France a short time earlier (6).

Conclusion

We report a case of fatal poisoning linked to the ingestion of powdered *Tabernanthe iboga* root. The overall analytical picture is consistent with a mixed overdose, with ibogaine as the toxic principle, in association with methadone and diazepam. The postmortem concentrations are consistent with this hypothesis when compared to data already published in the international scientific literature. Moreover, no cause of death was found at the autopsy either by macroscopic or histological analysis. The coroner's report concluded that the cause of death was iboga poisoning.

References

1. Alper KR. Ibogaine: a review. Alkaloids Chem Biol 2001;56:1–38.
2. Schultes RE, Hofmann A. Les plantes des dieux, les plantes hallucinogènes [Plants of the Gods, hallucinogenic plants]. Paris, France: Lezard, 2000.
3. Alper KR, Lotsof HS, Kaplan CD. The ibogaine medical subculture. J Ethnopharmacol 2008;115(1):9–24.
4. Sueur C, Benezech A, Deniau D, Lebeau B, Ziskind C. Les substances hallucinogènes et leurs usages en thérapeutiques. Revues de la littérature: partie 2 [Hallucinogenic substance and their use in therapeutics: part 2],

updated 1999; http://www.drogues.gouv.fr/fr/pdf/professionnels/ressources/dossier_halluci.pdf (accessed May 19, 2011).

5. Boucher A, Descottes J. Potentiel d'utilisation thérapeutique de l'ibogaöne: revue de la littérature. Lyon, France: C.E.I.P, 2006.

6. Kontrimavičiūtė V, Mathieu O, Mathieu-Daudé JC, Vainauskas P, Casper T, Baccino E, et al. Distribution of ibogaine and noribogaine in a man following a poisoning involving root bark of the *Tabernanthe iboga* shrub. J Anal Toxicol 2006;30(7):434–40.

7. Bogusz MJ, Maier RD, Krüger KD, Kohls U. Determination of common drugs of abuse in body fluids using one isolation procedure and liquid chromatography-atmospheric-pressure chemical-ionization mass spectrometry. J Anal Toxicol 1998;22(7):549–58.

8. Mash DC, Kovera CA, Buck BE, Norenberg MD, Shapshak P, Hearn WL, et al. Medication development of ibogaine as a pharmacotherapy for drug dependence. Ann N Y Acad Sci 1998;844:274–92.

9. Maas U, Strubelt S. Fatalities after taking ibogaine in addiction treatment could be related to sudden cardiac death caused by autonomic dysfunction. Med Hypotheses 2006;67(4):960–4.

10. Chèze M, Lenoan A, Deveaux M, Pépin G. Determination of ibogaine and noribogaine in biological fluids and hair by LC-MS/MS after *Tabernanthe iboga* abuse Iboga alkaloids distribution in a drowning death case. Forensic Sci Int 2008;176(1):58–66.

11. Table of ibogaine fatalities. Available from: http://www.myeboga.com/fatalities.html (accessed May 10, 2011).

12. Gallagher CA, Hough LB, Keefner SM, Seyed-Mozaffari A, Archer S, Glick SD. Identification and quantification of the indole alkaloid ibogaine in biological samples by gas chromatography-mass spectrometry. Biochem Pharmacol 1995;49(1):73–9.

13. Hearn WL, Pablo J, Hime GW, Mash DC. Identification and quantitation of ibogaine and an o-demethylated metabolite in brain and biological fluids using gas chromatography-mass spectrometry. J Anal Toxicol 1995;19(6):427–34.

14. Alburges ME, Foltz RL, Moody DE. Determination of ibogaine and 12-hydroxy-ibogamine in plasma by gas chromatography-positive ion chemical ionization-mass spectrometry. J Anal Toxicol 1995;19(6):381–6.

15. Ley FR, Jeffcoat AR, Thomas BF. Determination of ibogaine in plasma by gas chromatography-chemical ionization mass spectrometry. J Chromatogr A 1996;723(1):101–9.

16. Kontrimavičiūtė V, Breton H, Mathieu O, Mathieu-Daudé JC, Bressolle FM. Liquid chromatography-electrospray mass spectrometry determination of ibogaine and noribogaine in human plasma and whole blood. Application to poisoning involving *Tabernanthe iboga* root. J Chromatogr B Analyt Technol Biomed Life Sci 2006;843(2):131–41.

17. Björnstad K, Beck O, Helander A. A multi-component LC-MS/MS method for detection of ten plant-derived psychoactive substances in urine. J Chromatogr B Analyt Technol Biomed Life Sci 2009;877 (11–12):1162–8.

18. Gaillard Y, Pepin G. Use of high-performance liquid chromatography with photodiode-array UV detection for the creation of a 600-compound library. Application to forensic toxicology. J Chromatogr A 1997;2:149–63.

19. Hoelen DW, Spiering W, Valk GD. Long-QT syndrome induced by the antiaddiction drug ibogaine. N Engl J Med 2009;360(3):308–9.

20. Moffat A, Osselton M, Widdop B. Clarke's analysis of drugs and poisons in pharmaceuticals, body fluids and postmortem material, 3rd edn. London, UK: Pharmaceutical press, 2004.

21. Krantz MJ, Lewkowiez L, Hays H, Woodroffe MA, Robertson AD, Mehler PS. Torsade de pointes associated with very-high-dose methadone. Ann Intern Med 2002;137(6):501–4.

22. Krantz MJ, Martin J, Stimmel B, Mehta D, Haigney MC. QTc interval screening in methadone treatment. Ann Intern Med [Consensus Development Conference] 2009;150(6):387–95.

23. Ernst E, Bartu A, Popescu A, Ileutt KF, Hansson R, Plumley N. Methadone-related deaths in Western Australia 1993-99. Aust N Z J Public Health 2002;26(4):364–70.

24. Kuryshev YA, Bruening-Wright A, Brown AM, Kirsch GE. Increased cardiac risk in concomitant methadone and diazepam treatment: pharmacodynamic interactions in cardiac ion channels. J Cardiovasc Pharmacol [Research Support, Non-U.S. Gov't] 2010;56(4):420–30.

25. Kintz P. Toxicologie et pharmacologie médicolégales [Medicolegal toxicology and pharmacology]. Nancy, France: Elsevier France, 1998.

26. Baselt RC. Disposition of toxic drugs and chemicals in man, 6th edn. Foster city, CA: Biomedical Publications, 2002.

27. Vorpahl TE, Coe JI. Correlation of antemortem and postmortem digoxin levels. J Forensic Sci 1978;23(2):329–34.

28. Hargrove VM, McCutcheon JR. Comparison of drug concentrations taken from clamped and unclamped femoral vessels. J Anal Toxicol 2008;32(8):621–5.

Additional information and reprint requests:
Jérémy Carlier, M.Sc.
Laboratoire LAT LUMTOX
800 av. Marie Curie, Z.I. Jean Jaurès
07800 La Voulte-sur-Rhône
France
E-mail: j.carlier@latlumtox.com