Quantitation of *N,N*-Dimethyltryptamine and Harmala Alkaloids in Human Plasma after Oral Dosing with *Ayahuasca*

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Abstract

Harmine, harmaline, tetrahydroharmine (THH), and *N,N*-dimethyltryptamine (DMT) were quantitated in plasma from 15 healthy male volunteers after the ingestion of *ayahuasca*, a beverage that has been used for religious purposes in Brazil since pre-Columbian times. A growing awareness of the interest in this ancient shamanistic practice in modern urban cultures and the widespread popular dissemination of the inebriant effects and type and sources of the plant admixtures used to prepare the beverage have provided additional impetus for this study. The three harmala alkaloids were quantitated from protein-precipitated plasma by high-performance liquid chromatography using fluorescence detection. Recovery from blank human plasma was quantitative, and the limit of quantitation (LOQ) was below 2 ng/mL of plasma for each of the harmala alkaloids. Standard concentrations ranged from 10 to 250 ng/mL for harmine and THH and from 1.0 to 25.0 ng/mL for harmaline, respectively. Linearity was observed for harmine, harmaline, and THH within these respective ranges. The highest concentrations of harmala alkaloids in human plasma were found to be 222.3 ng/mL for harmine, 134.5 ng/mL for THH, and 9.4 ng/mL for harmaline. DMT was quantitated by gas chromatography using nitrogen–phosphorus detection after liquid–liquid extraction with diphenhydramine as an internal standard. DMT recovery was quantitative, and the limit of detection and LOQ were 0.5 and 5 ng/mL, respectively. Linearity for DMT was observed from 5 to 1000 ng/mL. The one-step extraction method for DMT and the protein precipitation method for the three harmala alkaloids afford rapid, sensitive, and quantitative analyses of these alkaloids with minimal analyte loss. The analytical methods also may be applicable to other matrices, including whole blood and urine samples and homogenized tissue specimens. These are the first reported observations of DMT and harmala alkaloids in plasma after ritual ingestion of *ayahuasca*.

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Introduction

The human use of shamanistic inebriants has its roots in early civilizations. Some scholars have suggested that many cultures from around the world owe their religious beliefs to the ingestion of natural products that alter states of consciousness (1). *Ayahuasca*, also known as *yajé*, *hoasca*, and *daime* as well as many other local names, has been used for medicoreligious purposes throughout the Amazon and Orinoco River Basins of South America since pre-Columbian times (2,3). Recently published works and monographs have commented on the central role of the ritual use of *ayahuasca* in indigenous religions of South America (1,3). After their humble beginnings in the Brazilian Amazon, contemporary religious groups have grown into major religious movements with thousands of members who ingest *ayahuasca* in a ritual context (3). A recent report from the Drug Enforcement Agency Special Testing and Research Laboratory described the seizure of a modest amount of *ayahuasca* (erroneously referred to as "Santo Daime") from a suspected cocaine laboratory on the Bolivian–Brazilian border (4). The popular television show "The X-Files" recently featured *ayahuasca* as an important theme in an episode titled "Teso dos Bichos".

Harmala alkaloids (Figure 1), decocted from the pounded woody vine *Banisteriopsis caapi*, form the basis of this beverage, and the vine is often soaked or boiled with additional plant admixtures to obtain "teas" that impart a variety of psychoactive effects (1,3). Although these beverages may contain other psychoactive agents, the presence of harmala alkaloids is the common feature (4–8). *N,N*-Dimethyltryptamine (DMT) is also found in most preparations of *ayahuasca*, typically through the addition of leaves from *Psychotria viridis* (1,3–8). DMT (Figure 1) is found in many plants (3) and animals, including humans (9). Although DMT is a short-acting psychotropic agent when administered parenterally (6), it is not orally active because of its rapid degradation by the enzyme monoamine

oxidase type-A (MAO-A) (10). In contrast, DMT in *ayahuasca* is orally active because the harmala alkaloids contained in the beverage reversibly inhibit the activity of MAO-A (3).

Although there have been no reported deaths as a direct consequence of intoxication, the harmala alkaloids in *ayahuasca* and analogous preparations are potent inhibitors of the enzyme MAO-A (10). Inhibitors of MAO (MAOIs) are known to precipitate adverse and even fatal drug reactions when combined with other medications, including the specific serotonin reuptake inhibitors (SSRIs) (11). The blockade of MAO metabolism by harmala alkaloids together with the decreased reuptake of neurotransmitter from the synapse by SSRIs may lead to development of a serotonin syndrome (12). With the recent increase in prescribed use of SSRIs and the growing interest in *ayahuasca* and related preparations (3), the risk of inadvertent toxicity due to the combined exposure to SSRIs and MAOIs has increased. An analytical procedure for the rapid detection of harmala alkaloids in plasma could be of use to the forensic toxicologist, especially in cases of unexplained serotonin syndrome in which consumption of illicit drugs is suspected (13).

Members of the União do Vegetal (UDV) and other syncretic churches in Brazil currently use *ayahuasca* as a sacrament in their religious practice. The use of this beverage for religious purposes has been protected by Brazilian law since 1987 (3). At the invitation of the UDV, a prospective study was undertaken to examine the immediate and long-term effects of ingesting oral doses of *ayahuasca*. Fifteen members of the UDV who had consumed *ayahuasca* on a regular (biweekly) basis in a ritual context for more than 10 years participated in a clinical and pharmacokinetic study of *ayahuasca*. We report here the development and application of two rapid, sensitive, and reliable analytical methods to extract and quantitate DMT by gas chromatography with nitrogen-phosphorus detection (GC–NPD) and the harmala alkaloids (harmine, harmaline, and tetrahydroharmine [THH]) by high-performance liquid chromatography (HPLC) with fluorescence detection in human plasma samples.

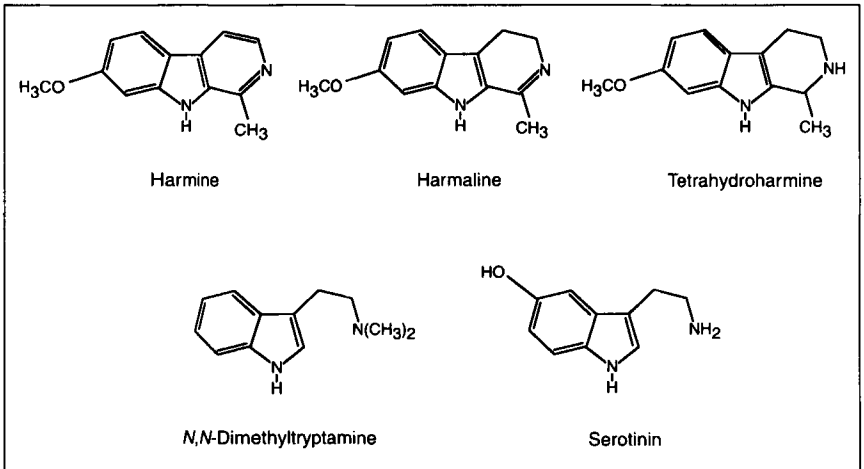

Figure 1. Molecular structures of *N,N*-dimethyltryptamine and harmala alkaloids found in *ayahuasca*. Serotonin is included to illustrate the molecular similarity to the other indole alkaloids.

Materials and Methods

Chemicals and reagents

Reagent-grade sodium carbonate and hydrochloric acid were obtained from J.T. Baker (Phillipsburg, NJ). *n*-Butyl chloride and methanol were obtained from Burdick & Jackson (Muskegon, MI) as distilled-in-glass-quality. High-purity HPLC-grade acetonitrile and methanol were obtained through Baxter, ammonium acetate (HPLC-grade) was purchased from Fisher Scientific, and water was taken from an in-house Nanopure II tap (Barnstead) to prepare the buffer for the mobile phase. Harmine, harmaline, and DMT were purchased from Sigma Chemical Co. (St. Louis, MO) as free bases. Harmaline was converted to the hydrochloride salt by the addition of 1M HCl. Diphenhydramine (DPH) hydrochloride (United States Pharmacopeia-grade) was provided by Abbott Laboratories (North Chicago, IL).

Synthesis of THH

Harmaline hydrochloride (502 mg, 2.0 mmol) was slowly added to a stirred suspension of $NaBH_4$ (76 mg, 2.0 mmol; Sigma) in CH_3OH at 0°C. After 40 min, the mixture was acidified with 1M HCl, then made alkaline with 5% aqueous NaOH and extracted with CH_2Cl_2 (J.T. Baker). The evaporated residue was twice recrystallized from EtOH (Alko Oy, Helsinki, Finland) to give an off-white powder (87% yield) with a melting point of 197–199°C.

Instrumentation

HPLC. A Perkin-Elmer Series 200 autosampler was used to control the entire HPLC system, which consisted of a PE series 410 LC pump with a Supelcosil LC-DB-8 column (15.0 × 4.6-mm i.d., 5-mm particle size) and two fluorescence detectors in tandem; a Perkin-Elmer LC-240 (fluorescence: excitation wavelength, λ = 232 nm; emission wavelength, λ = 351 nm) to measure harmine, THH, and DMT followed by a Kratos Analytical Spectroflow 980 (fluorescence: excitation wavelength, λ = 340 nm; emission wavelength, λ = 495 nm) to measure harmine and harmaline. Approximately 15 cm of HPLC tubing connected these two detectors, which gave a time delay of approximately 0.1 min for the second detector's response. The mobile phase was 20% methanol, 20% acetonitrile, and 60% 0.1M ammonium acetate, pH 6.9, at a flow rate of 2.0 mL/min.

GC. A Hewlett-Packard 5890 series II gas chromatograph with dual packed column inlets and dual NPDs was used to measure DMT. Two different capillary columns were used. Both were 15-m × 0.53-mm i.d. fused-silica Megabore® columns coated with either a 1.0-µm film thickness (DB-1) or a 1.5-µm film thickness (DB-17) stationary phase (J&W Scientific, Folsom, CA). The carrier gas was helium, and the flow rate was 15.4 mL/min. The injection ports and detectors were maintained at 250°C and 300°C, respectively. The oven temperature

was programmed as follows: initial temperature, 150°C; initial hold, 1.0 min; program rate, 10.0°C/min; final temperature, 270°C; and final hold, 0.10 min. The instrument was controlled by a workstation using Turbochrome™ software in a Digital DECpc LPv 466 d2 computer.

Mass spectra were obtained using a Finnigan MAT ITS-40 gas chromatograph–mass spectrometer (GC–MS) operated in the full-scan electron ionization mode or chemical ionization mode with methane reagent gas (Matheson Gas Products, Miami, FL); ions were scanned for in the range *m/z* 45–450 at 1.0 s per scan. The system used a high-performance Varian model 3400 GC with a 1075 split–splitless capillary injector in combination with an ion-trap mass spectrometer. The instrument was controlled by a workstation Gateway 2000 computer using Magnum™ software. A DB-5 phenylmethylsilicone fused-silica capillary column (15 m × 0.25-mm i.d., 0.1-µm film thickness; J&W Scientific) was used in the analysis. The manifold, injector, and transfer line temperatures were held at 220, 250, and 280°C, respectively. The oven temperature was programmed at 50°C for 1 min, then heated to 300°C at 15.0°C/min, and maintained at 300°C for 5.34 min. The carrier gas was helium, and the flow rate was 1 mL/min. The mass assignments were calibrated from *m/z* 33 to 650 using perfluorotributylamine (FC43), which was obtained from Scientific Instrument Services (Ringoes, NJ).

Calibration

Aliquots of blank plasma were spiked with concentrated amounts of the harmala alkaloids prepared in a mobile phase, and standard serial plasma dilutions were made from these concentrated plasma solutions to reduce the volume of the nonplasma matrix. A parallel set of standards was prepared as neat alkaloid dilutions in the mobile phase. Both sets were treated with cold acetonitrile and centrifugation. A comparison of extraction efficiency between these two sets was used to determine the recovery of alkaloid from plasma. Alkaloid concentrations were directly calculated from equations that described the standard curves using signal response versus concentration in nanograms-per-milliliter. For plasma analysis, the standards ranged from 10 to 250 ng/mL for THH and harmine and from 1.0 to 25.0 ng/mL for harmaline.

Calibration curves for DMT were prepared by spiking aliquots of plasma with methanolic working solutions of standards to yield final concentrations of 5–1000 ng/mL. The working range, when human samples were analyzed, was 5 – 50 ng/mL. Analyte concentrations were calculated by comparison with standard curves. DPH was used as the internal standard. Peak-area ratios (DMT/internal standard) were calculated using the Turbochrome software and subjected to least-squares linear regression. The resulting standard curve equation was used to calculate the concentrations of DMT in the plasma samples.

Sample collection

Whole blood was collected from a cubital vein of healthy adult men who were members of the UDV, a syncretic religion in Brazil, who had used *ayahuasca* as part of their religious practice for more than 10 years. Volunteers had no exposure to ayahuasca for at least seven days before the study. Plasma samples were collected at timed intervals for 8 h after the ingestion of *ayahuasca* (2 mL/kg body weight). The same batch of *ayahuasca* was used throughout the study. Using ethylenediaminetetraacetic acid as the anticoagulant, we isolated human plasma by centrifugation at 200 × *g* for 10 min at ambient Amazonian temperatures (33–38°C). Plasma samples were immediately frozen on dry ice and remained frozen at –80°C until analysis. All participants in this study were given a complete medical examination, and each gave written informed consent to participate. Blank human plasma was obtained from the South Florida American Red Cross (Miami, FL).

Sample preparation

For HPLC analysis, cold acetonitrile (0.5 mL, –35°C) was added to 0.5 mL of thawed plasma in a 1.5-mL Eppendorf tube. This mixture was vortex mixed for approximately 3 s and microcentrifuged (TDx, Abbot Laboratories) at 9500 × *g* for 5 min. The supernatant was directly decanted into a 1.0-mL glass injection vial, and 50 µL was injected for each analysis. For the HPLC alkaloid analysis of *ayahuasca,* a sample of the tea was simply diluted in the mobile phase (1:10), microcentrifuged, and injected (10 µL).

DMT was quantitated by GC–NPD using the following procedure: the sample (0.5 mL) was placed into a 15-mL silanized, round-bottom, screw-top glass tube, spiked with DPH (25 or 250 ng in 50 µL methanol), buffered to a pH greater than 10 with 2 mL saturated Na_2CO_3, and extracted with 7 mL *n*-butyl chloride by rotating for 30 min at room temperature. After centrifugation, the *n*-butyl chloride layer was transferred to a second tube with a conical bottom. A drop of methanolic HCl (1%, v/v) was added before evaporation to dryness at 40°C under N_2. The residue was reconstituted in 25 µL methanol for injection (2 µL) into the instrument.

Results and Discussion

Components of harmala alkaloids were identified by retention times and by co-injection of standards with selected experimental samples (50 ng/mL of added harmine or THH or 10 ng/mL harmaline) and further verified by their fluorescent characteristics using the two sets of established wavelengths. DMT was detected and quantitated in plasma samples by liquid–liquid extraction with DPH as an internal standard followed by GC–NPD. Spiked solvent samples were injected on a DB-1 column, and good chromatographic results for DMT were seen. However, when spiked control plasma samples were used, DMT coeluted with a large peak identified as caffeine by GC–MS (base peak at *m/z* 194, data not shown). Because caffeine would be a common contaminant in plasma samples, better separation of DMT from caffeine was achieved by using the more polar DB-17 column. The internal standard, DPH, which is also a tertiary amine, was chosen based on its retention time relative to DMT. Figure 2 illustrates two representative chromatograms from human plasma samples; Figure 2A is a chromatogram of a sample taken before administration of oral doses of *ayahuasca,* which shows a signal only for the internal

standard, and Figure 2B is a chromatogram of a sample taken 120 min after the consumption of *ayahuasca* (the ingested equivalent of 38.4 mg DMT), which demonstrates signals corresponding to plasma concentrations of 25.5 ng/mL DMT and 25 ng/mL DPH. DMT and the internal standard, DPH, had relative retention times of 5.3 and 5.7 min, respectively.

Method validation

Recovery. Harmala alkaloid recoveries were calculated from protein precipitation of 10 spiked plasma samples at 10 and 250 ng/mL for harmine and THH, respectively, and 1 and 15 ng/mL for harmaline. DMT recovery was calculated from the one-step alkaline liquid–liquid extraction of 10 spiked plasma samples at 10 and 20 ng/mL. The analyte recoveries were quantitative at both concentrations for all alkaloids. For DMT, quantitative recoveries were obtained provided the evaporation temperature was no higher than 40°C (data not shown).

Sensitivity. The sensitivity of an analytical method is defined by its limit of detection (LOD) and its limit of quantitation (LOQ). The LODs for the harmala alkaloids in the present HPLC assay were as follows: harmine, 0.1 ng/mL; harmaline, 0.05 ng/mL; and THH, 0.1 ng/mL. For DMT, the LOD with GC–NPD was 0.5 ng/mL. These values were determined from averages of 10 samples and were statistically significant with greater than 95% probability. For quantitative method validation, the LOQ was considered to be the lowest concentration of analyte in which the percent coefficient of variation (%CV) did not exceed 20%. The LOQs for the harmala alkaloids in the present HPLC assay were as follows: harmine, 2 ng/mL; harmaline, 1.0 ng/mL; and THH, 1.9 ng/mL. The LOQ of DMT for the GC–NPD assay was 5 ng/mL.

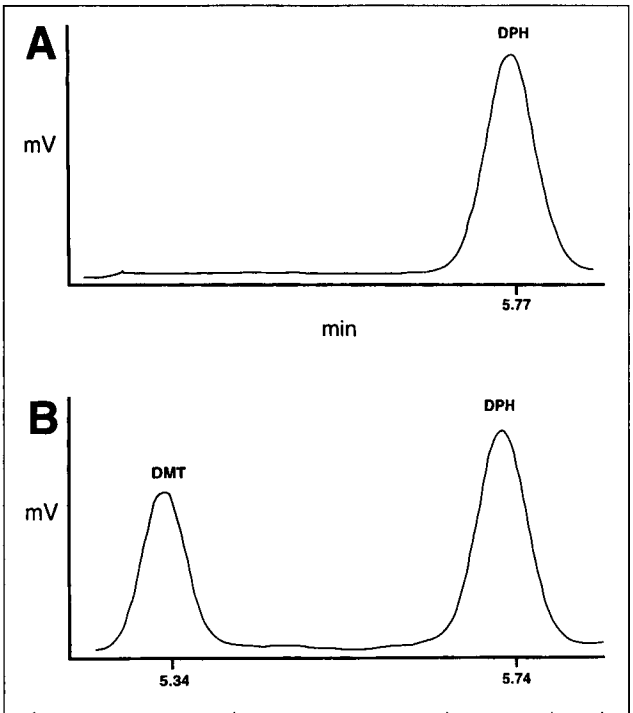

Figure 2. Representative chromatograms using gas chromatography with a nitrogen-phosphorus detector for analysis of *N,N*-dimethyltryptamine (DMT) from experimental plasma samples: (A) an extracted plasma sample before administration of *ayahuasca* with 25 ng/mL diphenhydramine (DPH) as an internal standard and (B) a sample from the same individual 120 min after ingestion, again with 25 ng/mL DPH as an internal standard and a signal corresponding to 25.5 ng/mL DMT.

Precision. The intra-assay precision for the harmala alkaloids, determined by a comparison of the %CVs of 10 replicate calculated concentrations, and all standards were calculated from three separate experiments. For harmine, the values obtained by HPLC were 3.54 and 7.23% at 10 and 250 ng/mL, respectively; harmaline values were 13.34 and 2.97% at 1 and 25 ng/mL, respectively; and THH values were 5.68 and 13.22% at 10 and 250 ng/mL, respectively. For the analysis of DMT by GC–NPD, the values were 6.84 and 8.48% at 10 and 20 ng/mL, respectively. The HPLC interassay precision values for harmine were 10.57 and 5.63% at 10 and 250 ng/mL, respectively; harmaline values were 13.33 and 2.73% at 1 and 25 ng/mL; and THH values were 5.37 and 11.59% at 10 and 250 ng/mL, respectively. For the analysis of DMT, these values were determined to be 2.47 and 6.11% for 10 and 20 ng/mL, respectively.

Accuracy. The accuracies of the assays were determined in parallel with the precision studies described. Ten replicate samples gave a mean of 10.8 ± 0.3 ng/mL and 265.21 ± 1.3 ng/mL at 10 and 250 ng/mL, respectively, for harmine; 1.1 ± 0.2 ng/mL and 15.34 ± 0.3 ng/mL at 1 and 15 ng/mL, respectively, for harmaline; 9.83 ± 0.2 ng/mL and 273.93 ± 3.5 ng/mL at 10 and 250 ng/mL, respectively, for THH, for the HPLC analyses, and 11.8 ± 0.6 ng/mL and 22.2 ± 0.4 ng/mL at 10 and 20 ng/mL, respectively, for DMT. The variation was less than 20%.

Linearity

The linearity was determined for the three harmala alkaloids by diluting 100-mg/mL solutions of each alkaloid in the mobile phase and preparing spiked plasma samples from these solutions to concentrations of 10, 25, 50, 125, and 250 ng/mL for harmine and THH and 1, 2.5, 5, 10, and 25 ng/mL for harmaline. Each standard was taken through the preparation procedure and assayed by injecting 50 µL. Initial calculations gave recoveries just over 100% when spiked plasma samples were compared with pure alkaloids diluted in mobile phase, perhaps because of an overestimation based on a slight loss in precipitated protein from the plasma samples.

For DMT analysis by GC–NPD, the concentration–response relationship was defined by a linear regression of peak area versus concentration of DMT. All standard curves were prepared by spiking known amounts of DMT in blank plasma samples and coextracting them with the experimental samples. For assay method validation, the linearity was measured initially up to 1000 ng/mL. Standard curves were generated with the following concentrations: 5, 10, 50, 100, 500, and 1000 ng/mL; the internal standard, DPH, had a concentration of 250 ng/mL. The standard curves were found to be linear (coefficient of determination [r^2], 0.996) across this concentration range. However, the plasma samples taken for the study had DMT concentrations that ranged between 10 and 25 ng/mL. Based on this initial assessment, the working range was chosen to be 5–50 ng/mL, and the internal standard was at 25 ng/mL. Least-squares regression analysis gave an r^2 value of 0.994. The linear relationship between concentration and response was reproducible across all experimental runs.

Two detectors in tandem

Although the Perkin-Elmer LC 240 fluorescence detector can be programmed to change wavelengths during chromatographic analysis, it can only monitor one set of wavelengths (emission or excitation) at any given time. Using two detectors allowed for the simultaneous quantitation of harmine with either THH (emission/excitation wavelength, 232/351 nm) or harmaline (340/495 nm). Only harmaline was quantitated at emission/excitation wavelengths of 340/495 nm, and harmine was found to be approximately 5 times more sensitive at emission/excitation wavelengths of 232/351 nm. Figure 3 shows typical chromatograms of an actual sample (Figure 3A and 3C) and standards (Figure 3B and 3D) observed at emission/excitation wavelengths of 232/351 nm (Figure 3A and 3B) and 340/495 nm (Figure 3C and 3D).

DMT was found to be a major component of this beverage. In the HPLC analysis, DMT could be resolved as a single peak, although it was not strongly fluorescent at emission/excitation wavelengths of 232/351 nm (LOD, 20 ng/mL) and was essentially undetected at emission/excitation wavelengths of 340/495 nm. Like harmaline, the DMT concentration was relatively low in the *ayahuasca* tea. Moreover, the retention time of DMT (6.2 min) did not coincide with any of the signals for the harmala alkaloids under these conditions. Although DMT was not detected in any of the plasma samples, it was quantitated from the single batch of tea that was used in this study and verified by GC–NPD (data not shown).

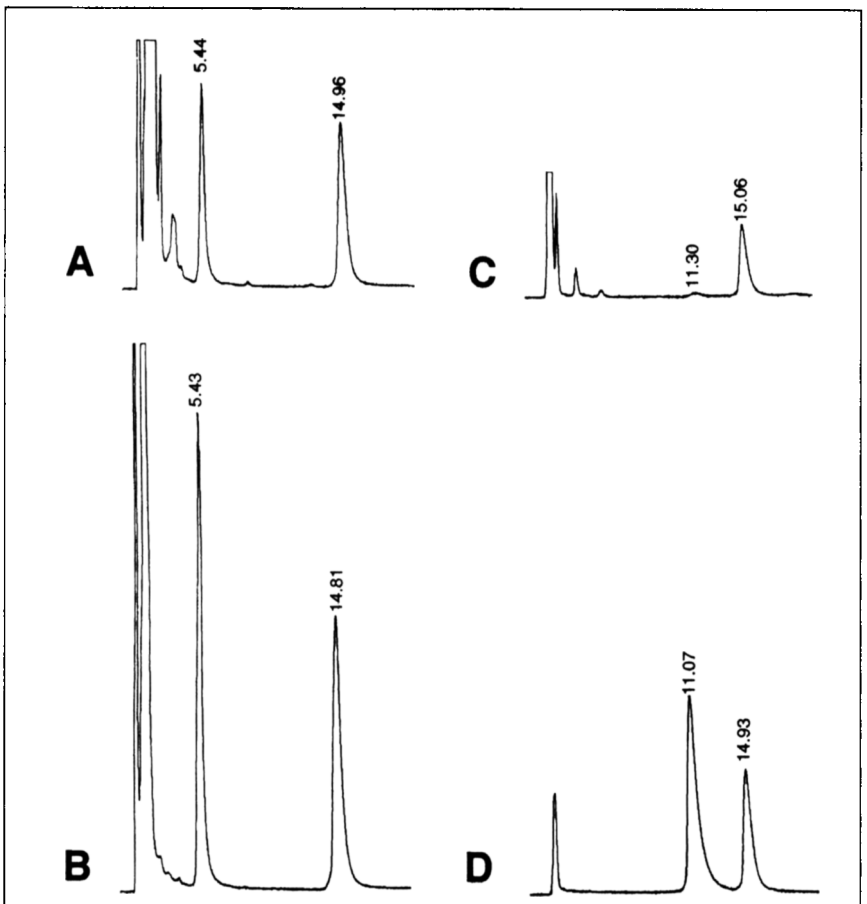

Figure 3. Chromatograms of harmala alkaloids detected at (A and B) an excitation wavelength of 232 nm and an emission wavelength of 351 nm and (C and D) an excitation wavelength of 340 nm and an emission wavelength of 495 nm, showing (A and C) an actual sample taken 120 min after the ingestion of *ayahuasca* and (B and D) a sample of spiked plasma.

Application of the analytical methods

The analytical procedures were applied to a pharmacokinetic study of DMT and harmala alkaloid concentrations in plasma from 15 healthy male volunteers after they ingested 2 mL/kg body weight from the same batch of *ayahuasca*. The *ayahuasca* used in this study was analyzed for concentrations of harmine (1.70 mg/mL), harmaline (0.2 mg/mL), THH (1.07 mg/mL), and DMT (0.24 mg/mL) using the methods described here. Thus, for a 59-kg individual, the average oral doses of *ayahuasca* alkaloids ingested were as follows: harmine, 204.0 mg; harmaline, 24.0 mg; THH, 128.4 mg; and DMT, 28.8 mg. These concentrations in the tea resulted in the following peak plasma concentrations (C_{max}) in a representative individual volunteer: harmine, 92.3 ng/mL; harmaline, less than 1.0 ng/mL; THH, 82.2 ng/mL; and DMT, 12.4 ng/mL (Figure 4). The range and average values for the 15 subjects are shown in Table I.

Although harmaline was detected in some volunteers, values for C_{max} were only reliably determined in six of the 15 volunteers. This finding most likely reflects the low levels of harmaline contained in the tea (0.2 mg/mL) and, perhaps in part, to individual differences in absorption and metabolism. In previous reports (6,14), peak plasma levels of DMT after intravenous administration occurred after 2 min, then rapidly dropped to baseline levels by 30 min. Peak plasma DMT levels were reported to correspond with peak psychoactivity after intravenous administration (15). In the present study, we observed a similar range for DMT levels in plasma after oral ingestion of the tea. Although the psychoactivity was reportedly much less intense, the psychoactive effects lasted for a longer duration with oral doses than with intravenous administrations. These preliminary observations suggest that the time course for the appearance of the subjective effects most closely follows the DMT pharmacokinetic profile shown in Figure 4. Unlike the reported "rush" associated with the rapid rise in plasma DMT concentrations after intravenous doses, the oral doses produced mild responses that were typically associated with the known spectrum of psychedelic effects demonstrated with intravenous administrations of DMT (6,15). Harmala alkaloids are well-known inhibitors of MAO-A enzymes, for which DMT is a substrate (10). The more extended profiles seen for DMT levels in the plasma after ingestion of *ayahuasca* are best explained by the actions of harmala alkaloids, which inhibit the metabolism of DMT by MAO-A.

Conclusion

Evaluation of the effects of *ayahuasca* in human volunteers required the development of analytical methods to quantitate DMT and harmala alkaloids in plasma samples. The analytical methods described here provide accurate and reliable quantitative assays of DMT and harmala alkaloids in human plasma samples and may be applicable to other matrices, including whole blood, urine, and tissue homogenates. Hallucinogens produce a unique syndrome of psychological effects in humans and cause alterations in perceptual and cognitive processes that make it difficult to maintain a clear sensorium (6). The application of the analytical procedures for measurement of DMT, harmaline, and THH will contribute to the understanding of the subjective dose effects and the pharmacodynamic and pharmacokinetic profiles of *ayahuasca* alkaloids in human subjects.

Because of the rising popularity of *ayahuasca* and other plant inebriant beverages and the current widespread use of Prozac and other SSRIs in North America and Europe, there is the possibility of inadvertent coadministration of MAOIs with an SSRI; therefore, there is a concern about potentially serious toxicities associated with the emergence of a serotonin syndrome. This potentially lethal condition is especially insidious given the long half-life of active SSRI metabolites, which may precipitate a serotonin syndrome several weeks after cessation of the administration of the parent drug (16).

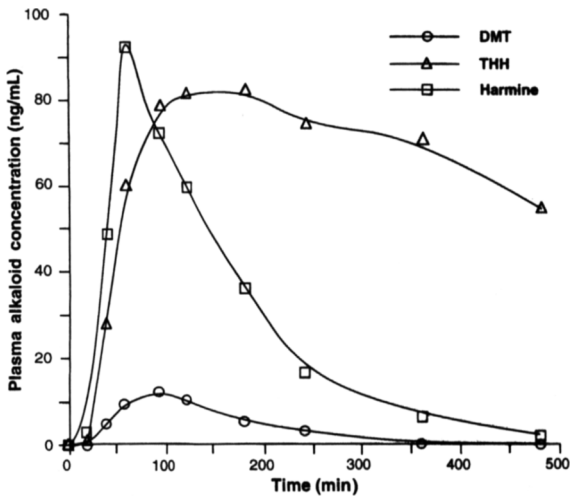

Figure 4. Representative pharmacokinetic profiles of plasma alkaloids over time from the same individual. This volunteer (59 kg) ingested 120 mL of *ayahuasca*, which corresponds to a total consumption of 204.0 mg harmine, 24.0 mg harmaline, 128.4 mg tetrahydroharmine (THH), and 28.8 mg *N,N*-dimethyltryptamine (DMT).

Table I. Range and Average (Plus or Minus Standard Error) Values for Peak Concentrations of DMT and Harmala Alkaloids in 15 Men after Oral Doses of *Ayahuasca*

	DMT* (ng/mL)	THH† (ng/mL)	Harmaline (ng/mL)	Harmine (ng/mL)
Range	11.5–25.5	49.2–134.5	<1.0–9.4	36.4–222.3
Average	15.8 ± 1.1	90.8 ± 5.9	6.2 ± 0.9	114.6 ± 16.5

* DMT = N,N-Dimethyltryptamine.
† THH = Tetrahydroharmine.

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