Associate editor: B.L. Roth

Hallucinogens and dissociative agents naturally growing in the United States

John H. Halpern*

Biological Psychiatry Laboratory, Alcohol and Drug Abuse Research Center, Harvard Medical School, McLean Hospital, 115 Mill Street, Belmont, MA 02478-9106, USA

Abstract

It is usually believed that drugs of abuse are smuggled into the United States or are clandestinely produced for illicit distribution. Less well known is that many hallucinogens and dissociative agents can be obtained from plants and fungi growing wild or in gardens. Some of these botanical sources can be located throughout the United States; others have a more narrow distribution. This article reviews plants containing N,N-dimethyltryptamine, reversible type A monoamine oxidase inhibitors (MAOI), lysergic acid amide, the anticholinergic drugs atropine and scopolamine, or the diterpene salvinorin-A (*Salvia divinorum*). Also reviewed are mescaline-containing cacti, psilocybin/psilocin-containing mushrooms, and the *Amanita muscaria* and *Amanita pantherina* mushrooms that contain muscimol and ibotenic acid. Dangerous misidentification is most common with the mushrooms, but even a novice forager can quickly learn how to properly identify and prepare for ingestion many of these plants. Moreover, through the ever-expanding dissemination of information via the Internet, this knowledge is being obtained and acted upon by more and more individuals. This general overview includes information on the geographical range, drug content, preparation, intoxication, and the special health risks associated with some of these plants. Information is also offered on the unique issue of when bona fide religions use such plants as sacraments in the United States. In addition to the Native American Church's (NAC) longstanding right to peyote, two religions of Brazilian origin, the Santo Daime and the Uniao do Vegetal (UDV), are seeking legal protection in the United States for their use of sacramental dimethyltryptamine-containing "ayahuasca."
© 2004 Elsevier Inc. All rights reserved.

Keywords: Plants; Hallucinogens; Drug use; Intoxication; Religion; Anticholinergic

Contents

* Tel.: 617-855-3703; fax: 617-855-3585.
E-mail address: john_halpern@hms.harvard.edu (J.H. Halpern).

1. Introduction

A determined individual can almost anywhere locate naturally occurring plant-based poisons, chemicals, and medications—some of which are psychoactive (Schultes, 1969; Carlini, 2003). Excluding wild nicotine–containing tobaccos and the intentional production of *Cannabis* spp., most psychoactive drugs found naturally in the United States are hallucinogenic and/or dissociative intoxicants. Some of these drugs are emerging drugs of abuse, others are contained in plants that have never been traditionally or popularly sought out as intoxicants, but, in all cases, these drugs are relatively easy to identify and have a well-defined geographical distribution. Clinicians, educators, policymakers, and parents need to be especially mindful of the existence of native intoxicants because the use of hallucinogens by young Americans has increased dramatically over the past decade (Johnston et al., 2003) and because the dissemination of information about these intoxicants has been aided through the ever-expanding Internet (Halpern & Pope, 2001).

This article reviews the geographic distribution, preparation, intoxication, pertinent special legal issues, and basic pharmacology of plants containing *N,N*-dimethyltryptamine (DMT) (*Psychotria viridis*, *Desmanthus illinoensis*, *Phalaris arundinacea*, *Phalaris aquatica*, and *Phalaris tuberosa*), reversible monoamine oxidase A inhibitors (MAOI) (*Banisteriopsis caapi*, *Peganum harmala*, and *Passiflora incarnata*), psilocybin and psilocin (*Psilocybe cubensis* and other spp.), mescaline (*Lophophoria williamsii*, *Trichocereus pachanoi*, and *Trichocereus peruvianus*), salvinorin-A (*Salvia divinorum*), lysergic acid amide (*Argyreia nervosa*, *Ipomoea violacea*, and *Stipa robusta*), atropine and scopolamine (*Datura stamonium*, *Atropa belladonna*, *Hyoscyamus niger*, and *Mandragora officinarum*), and muscimol and ibotenic acid (the *Amanita muscaria* and *Amanita pantherina* mushrooms). This article is based in part on a lecture given at the National Institute on Drug Abuse and Office of Natural Products sponsored workshop "Psychoactive Botanical Products": the lecture's slide presentation is available online with additional information on *Ephedra* spp. and the *Bufo alvarius* frog (http://www.drugabuse.gov/whatsnew/meetings/psychoactivemtgsumm.html).

2. *N,N*-Dimethyltryptamine and reversible monoamine oxidase inhibitors

Indigenous peoples of the Amazon have used DMT for spiritual and medicinal purposes for thousands of years (Schultes & Hofmann, 1992). South American powdered snuffs are usually prepared from the seeds of *Anadenanthera peregrina* or the bark of *Virola* spp. trees, but there are many other botanical sources for DMT in South America and elsewhere (Schultes & Hofmann, 1992). Probably the most common South American ethnomedicine to contain DMT is the brewed tea "ayahuasca." Hallucinogenic when smoked, inhaled, injected, or as an enema, DMT is orally active only when monoamine oxidase enzymes in the gut and liver are inhibited. Ayahuasca contains enough reversible type A MAOI (from the vine *Banisteriopsis caapi*) for DMT (from the leaves of the plant *Psychotria viridis*) to impart a 3- to 4-hr intoxication that peaks in subjective intensity within the first hour (Riba et al., 2001). Specifically, the MAOI found in ayahuasca are the β-carbolines harmaline, harmine, and 1,2,3,4-tetrahydroharmine, all of which are also reported to have mild sedative and hallucinogenic properties (Pennes & Hoch, 1957; Slotkin et al., 1970; Naranjo, 1979; Turner, 1994; Shulgin & Shulgin, 1997; Grella et al., 1998). Although alkaloid content varies across batches and specific recipes, one study reported that an average 100-mL dose of ayahuasca contained 24 mg of DMT, 107 mg of 1,2,3,4-tetrahydroharmine, 20 mg of harmaline, and 170 mg of harmine (Callaway et al., 1996). The β-carboline MAOI contained in *Banisteriopsis caapi* range from 0.05% to 1.95% by dry weight and the DMT in *Psychotria viridis* ranges from 0.1% to 0.66% by dry weight (Rivier & Lindgren, 1972; McKenna et al., 1984).

In the United States, DMT has never been a common drug of abuse. Illicit DMT is either a natural extract or synthetic powder. In the 1960s, it was sometimes referred to as the "businessman's trip" (during a lunch break, for example), because smoked DMT rapidly intoxicates with a peak achieved within 2–5 min and then clearing over the next 20–30 min (see http://www.usdoj.gov/dea/concern/psilocybin.html). Typically, 40–50 mg is smoked, but anecdotal reports exist describing use from 20 to as much as 100 mg of DMT (Shulgin & Shulgin, 1997). The effective intravenous dosage range has been estimated to be 0.1–0.4 mg/kg (Strassman, 1996); 0.6 mg/kg was observed to be "too much" and difficult to recollect for two research participants (Strassman, 2001).

DMT can be found in common plants growing in much of the United States. In particular, appreciable amounts of DMT can be obtained through simple juice extraction of *Phalaris arundinacea*, *Phalaris tuberosa*, or *Phalaris aquatica* (canary grass), which are often found in fallow fields, cracks in sidewalks, and many lawns across the entire United States (USDA, 2004). DMT content is highly variable in *Phalaris* spp. (Baxter & Slaytor, 1972; Barker & Hovin, 1974; Mack et al., 1988), but high percentage strains can be ordered through the Internet (Halpern & Pope, 2001). *Desmanthus illinoensis* (prairie bundleflower) also has a wide American distribution (USDA, 2004); the root bark of this prairie legume has been found to contain 0.34% DMT (Thompson et al., 1987).

It is unlikely that DMT will ever become a major drug of abuse; it is physiologically nonaddictive and the MAOI contained in its orally active preparations, such as ayahuasca, lead to nausea and vomiting that routinely follows consumption. Law enforcement measures might not be

capable of controlling DMT use, however, should these local plants become popular "manufacture" sources. Moreover, Amazonian plants are not needed for rendering DMT orally active; the same β-carboline MAOI contained in ayahuasca are also found in *Peganum harmala* (Syrian rue) and *Passiflora incarnata* (passionflower). *Peganum harmala* was introduced into the western United States and is now found in the wild (USDA, 2004); it has 2–4% MAOI content by dry weight (McKenna et al., 1984). *Passiflora incarnata* grows throughout the Southeast and much of the Midwest (USDA, 2004) and has ~ 1% MAOI content. *Passiflora* is used in some herbal preparations for its sedative properties and it bears an edible fruit. Nontraditional boiled brews from these American-sourced plants are not theoretical: recipes can be found on the Internet and self-reports appear to confirm that they are ayahuasca approximations (see http://www.erowid.com and http://www.troutsnotes.com).

Popular interest in DMT is reemerging in the United States in part because sacramental ayahuasca use is no longer exclusive to the traditional shamanic practices of the surviving indigenous peoples of the Amazon Basin. For example, Columbia, Peru, and Brazil now have a number of "eco-tour" operations that intentionally make available an ayahuasca experience as part of a travel package for those seeking "spiritual awakening" and/or have adventurous curiosity about the Amazon. More significant, however, is the advent in the 20th century of religions that syncretize elements of Christianity with the traditional practices, ceremonies, and beliefs of ayahuasca-using native peoples. The two largest and best known of these religions are the Santo Daime and the Uniao do Vegetal (UDV), both of which have a clear Christian identity and are seeking legal protection for their religious use of ayahuasca in the United States (more below). Like the Native American Church (NAC), these religions of Brazilian origin conduct arduous, all-night services in conjunction with ingestion of their psychoactive sacrament.

A pilot survey assessing the psychological and general health of 15 male UDV members residing in Brazil failed to find any adverse health consequences from use of ayahuasca and recommended further research into claims of health benefits (Grob et al., 1996). Similar to the positive findings for using lysergic acid diethylamide (LSD) and other hallucinogens for the treatment of alcoholism and heroin addiction (Hoffer & Osmond, 1968; Halpern, 1996), members of these faiths assert that ayahuasca assisted their recovery from addiction to alcohol and other drugs (de Rios et al., 2002). Although one research team in Spain has been conducting basic clinical investigations of ayahuasca (Riba et al., 2002a, 2002b, 2003), very little research has been conducted on questions of purported benefits or possible harms from human ayahuasca use. Although disregarded perhaps out of persisting Western ethnocentricity, the ayahuasca-using native peoples of South America do have a several thousand-year history of safety with ayahuasca.

3. *Psilocybe* species mushrooms

Psilocybe cubensis and other species ("magic mushrooms") contain the hallucinogens psilocybin (4-phosphoryloxy-*N*,*N*-dimethyltryptamine) and psilocin (4-hydroxy-*N*,*N*-dimethyltryptamine). Although labeled toxic because they are psychoactive, these mushrooms are not lethal and are not known to induce internal organ damage—although misidentification sometimes results in the ingestion of mushrooms that are quite poisonous (Arora, 1990).

Psilocybe spp. are found in many regions of the world (Stamets, 1996). In the United States, these mushrooms are coprophagous, growing on cow and horse manure in the pastures of Florida through the southern Gulf States to Texas, in pasture and grain fields, and along the coastline of the Pacific Northwest from California into Canada. Some of the indigenous tribes in the Oaxaca region of Mexico still consider these mushrooms sacred; sacramental use extends historically back to the reign of the Aztec and earlier (Wasson, 1961).

Total psilocybin content varies with mushroom, subspecies, and preparation, but the most common mushroom, *Psilocybe cubensis*, typically contains 10–12 mg psilocybin/g dried mushroom (Stamets, 1996; Musshoff et al., 2000). Psilocybin is metabolized in the gut into psilocin, so psilocin is the actual intoxicating drug (Lindenblatt et al., 1998). Although *Psilocybe* spp. mushrooms, psilocybin, and psilocin are Schedule I drugs in the United States, mushroom spore prints remain legal (except in California). A small industry continues to supply mycologists and those interested in obtaining hallucinogens with the necessary materials to grow these mushrooms, which, of course, removes the risk of false identification and potential poisoning when wild-sourced.

Intoxication from *Psilocybe* spp. peaks within the first 2 hr, diminishing over the subsequent 3–4 hr. Approximately 40 μg psilocybin/kg body weight results in a threshold intoxication; typically 1–2 g of dried mushroom is ingested, which yields anywhere from 4 to 20 mg of psilocybin (Stamets, 1996). Cross-tolerance occurs between LSD and psilocybin/psilocin, but not as readily as between LSD and mescaline (Isbell et al., 1961).

4. Peyote

The peyote cactus, *Lophophoria williamsii*, contains over 60 alkaloids, but mescaline (β-3,4,5-trimethoxyphenethylamine) is its principal hallucinogenic constituent (1.5% mescaline by dry weight) (Kapadia & Fayez, 1973). Peyote grows within a narrow strip of desert along the Texas-Mexico border, pushing deeply into Mexico's Chihuahua desert. Spineless and slow growing, peyote has a small crown visible above the earth and a tuberous "carrot-like" root extending below. When properly cut, the crown ("button") is removed from the plant leaving the root intact.

Eventually, the root will sprout several new crowns that may be reharvested. Peyote is not smoked but eaten as peeled fresh buttons, dried whole buttons, dried/ground powder (sometimes also reconstituted with water), or is steeped/reconstituted into a warm tea. Consumption of pickled peyote sometimes occurs but is an uncommon practice since a case of botulism poisoning was reported (Hashimoto et al., 1998).

Peyote has a bitter, acrid taste, typically inducing nausea and vomiting in the novice initiate or when consumed in larger doses. A potent mescaline intoxication is ~ 3.75 mg/kg body weight. Peak intoxication occurs within 2–4 hr, wearing off over the subsequent 4–6 hr.

Peyote is most commonly consumed as a sacrament in the all-night ceremonies of the NAC, although NAC members also sometimes ingest peyote outside of the ceremonial setting as a continuing act of faith and as a medicine promoting good physical and mental wellbeing (Stewart, 1987). The NAC has ~ 300,000 members in the United States and Canada, making it the largest faith of Native Americans (see below for further discussion of legal status). Members can practice other traditional and religious beliefs, but the use of all drugs and alcohol is proscribed. Meetings are most often held on Saturdays and around special holidays. Ceremonies bring together families, neighbors, special guests, and other well-wishers, and sometimes visitors from afar (the NAC is pan-tribal), who pray throughout the night under the guidance of a priest "Road Chief" ("Road Man") while remaining in a tipi or other traditional structure. Much like the prayer meetings of other religions, these ceremonies may be called for special purposes, such as for the health of a loved one, a child returning to college, a birthday, important conflict resolution within the family, or for the safety of relatives serving in the military. Peyote is not forced on anyone in attendance but is freely offered and ingested. As little as a few drops of peyote tea might get placed on a child's lips as a blessing; the typical adult dose is a few teaspoons to many more, but, as this is the nondrug sacramental use of peyote, dosage is not scientifically measured. After morning prayers are completed and ceremonial water and food is blessed and then eaten by the congregants, a feast that has been prepared through the night by supporting relatives is served to all. Attendance varies like other religions; some members participate in peyote ceremonies once or twice a year or less while others might participate weekly or sometimes with greater frequency. On average, attendance is monthly.

5. Other mescaline-containing cacti

Mescaline is not exclusive to the peyote cactus. Indeed, there are many other mescaline-containing cacti, some of which have also been used in traditional ceremonies of indigenous peoples in South America, especially Peru. The two most common of these cacti are *Trichocereus pachanoi* (San Pedro) and *Trichocereus peruvianus* (Peruvian torch). Although not indigenous to the United States, these *Trichocereus* cacti are very common ornamental plants and can be purchased from garden shops across the country. *Trichocereus pachanoi* has been found to contain anywhere from 0.33% (Crosby & McLaughlin, 1973) to 2.375% (Helmlin & Brenneisen, 1992) mescaline by dry weight and *Trichocereus peruvianus* contained 0% (Agurell, 1969) to 0.82% (Pardanani et al., 1977). Typically, these cacti are boiled down into a soupy consistency for ingestion; emesis is even more likely than with peyote because of the large volume of plant material used.

6. *Salvia divinorum*

Salvia divinorum is from the mint family (*Lamiaceae*) and contains the psychoactive neoclerodane diterpene salvinorin-A. Most hallucinogens are psychoactive in part because of their action at the 5-HT$_{2A}$ serotonin receptor subtype, but salvinorin-A has no such activity and instead is the first known example of a naturally occurring nonnitrogenous κ-opioid receptor agonist (Roth et al., 2002). Traditionally consumed by Mazatec Indians of Oaxaca, Mexico, by chewing fresh leaves or by drinking the juice of the leaves for absorption of salvinorin-A through the oral mucosa (Valdes et al., 1983), these plants are now grown and sold in the United States for ingestion by people who obviously do not have a historical ceremonial connection to this plant. The leaves are sometimes smoked, but these new consumers are also purchasing concentrated extracts of the plant through Internet-based companies and smoke shops (Halpern & Pope, 2001). When smoked, salvinorin-A is psychoactive for 15 min at doses of 200–500 μg (Siebert, 1994); oral absorption leads to a less intense intoxication lasting up to 1 hr. Although the Drug Enforcement Administration (DEA) has not scheduled *Salvia divinorum*, they are closely monitoring it as a possibly emerging drug of abuse (National Drug Intelligence Center, 2003). With no reinforcing properties, harm from *Salvia divinorum* most likely occurs from inadequate preparation or from settings in which it is dangerous to be intoxicated with any drug at all (e.g., such as driving).

Many other *Lamiaceae* ornamentals may ultimately prove to be psychoactive similar to *Salvia divinorum*, including *Coleus* spp. plants that are very popular in gardens and prized for their intense leaf colors. Indeed, leaves of *Coleus blumei* and *Coleus pumilus* are sometimes chewed by Mazatec Indians instead of *Salvia divinorum* (Wasson, 1962; Schultes & Hofmann, 1992), although to date, only *Salvia divinorum* has been found to contain salvinorin-A. A more determined search for a *Salvia divinorum* substitute might be triggered by placement of *Salvia divinorum* into Schedule I. If such a plant exists, a whole Pandora's box of legal nightmares might be unleashed in trying to restrict popular access to these common houseplants.

7. Lysergic acid amide–containing plants

LSD is the best-known synthetic hallucinogen and is psychoactive at the microgram level. Although LSD does not occur in nature, a close analogue, lysergic acid amide (LSA, "ergine") is found in the seeds of *Argyreia nervosa* (Hawaiian baby woodrose) and *Ipomoea violacea* (morning glory). Hallucinogenic activity of LSA occurs with 2–5 mg, which provides a 4- to 8-hr intoxication that reportedly has quantitative as well as qualitative differences from LSD (Schultes & Hofmann, 1980). Seeds are crushed, germinated, eaten whole, or an extract is drunk after the seeds are soaked in water. Five to 10 seeds of *Argyreia nervosa* or 150–200 seeds (3–6 g) of *Ipomoea violacea* yield average doses of LSA (Al Assmar, 1999; Borsutzky et al., 2002). The LSA content of *Argyreia nervosa* is 0.14% by dry weight of seeds (Chao & Der Marderosian, 1973) and is 0.02% by dry weight in *Ipomoea violacea* seeds (Miller, 1970). Historically, *Ipomoea violacea* and related *Ipomoea corymbosa* seeds were used in Central America for shamanic and ceremonial purposes and the Mazatec of Mexico also continue their usage (Schultes & Hofmann, 1992). *Ipomoea* spp. are popular annuals grown for their abundant flowers from climbing vines; commercial seeds are usually coated with emetic poisons to discourage intoxication. The highest concentrations of LSA, however, have been found in *Stipa robusta* (*Achnatherum robustum*; sleepygrass) growing in the southwest of the United States (USDA, 2004), although there is no history of shamanic tradition with it and no evidence to date that it is commonly ingested for intoxication (Petroski et al., 1992).

8. Atropine- and scopolamine-containing plants

Atropine and scopolamine are competitive antagonists of muscarinic cholinergic receptors and are central nervous system depressants (Brown & Taylor, 2001). Approved medications, these drugs are used for dilating pupils for fundoscopy and are used in anesthesia to treat/prevent bradycardia and to decrease bronchial and salivary secretions. Atropine also is one of the medicines used for treating organophosphate poisoning and exposure to nerve agent chemical weapons. Scopolamine is a common treatment for motion sickness.

In overdose, these drugs induce a toxic delirium marked by pronounced anterograde amnesia, confusion, dissociation, hallucinations, delusions, and an excited, giddy affect (Ardila & Moreno, 1991). Coordination is also impaired, vision becomes blurry with increasing pupillary dilation, and overly dry mucous membranes may make it difficult to talk or swallow. Overdose can be lethal with fever, tachycardia, and arrhythmia. Reports of bizarre self-injury are not uncommon because the intoxication lasts for many hours, or even days, and the delirium can induce a dramatic disconnection from reality. Some symptoms, such as headache and pupillary dilation, may persist for days or weeks. The frighteningly adverse profile of overdose usually precludes common recreational abuse of these drugs or the plants that contain them (Grinspoon & Bakalar, 1997).

Scopolamine and atropine are also described as euphorogenic, and their shamanic use has occurred amongst Native Americans as well as indigenous peoples throughout the world (Kluckhohn, 1944; Grinspoon & Bakalar, 1997). Many plants and trees of the Solanacea family contain these compounds as well as a number of other anticholinergic alkaloids. Well-known plants include *Datura stamonium* (Jimson weed), *Atropa belladonna* (deadly nightshade), and *Mandragora officinarum* (Mandrake), which contain atropine and scopolamine, whereas *Hyoscyamus niger* (henbane) contains scopolamine without atropine (Arnett, 1995; Brown & Taylor, 2001). Most of these plants were introduced into the United States as ornamental flowers, but *Datura* spp. grow wild throughout the United States except for Wyoming and Alaska (USDA, 2004). Smoking or eating the leaves results in intoxication, but dangerous overdose is possible from the rest of the plant, as well, with the seeds being particularly toxic.

9. *Amanita muscaria* and *Amanita pantherina*

There are many varieties of *Amanita* and some of them are deadly poisonous (e.g., *Amanita phalloides*). *Amanita muscaria* (fly agaric) and *Amanita pantherina* (panther cap), if properly identified, are usually not toxic to the liver, but reactions are quite dependent on the individual and overdose is sometimes lethal. The key psychoactive constituents in these mushrooms are ibotenic acid, muscimol, and muscazone. A γ-aminobutyric acid receptor agonist, muscimol, is mildly sedating. Ibotenic acid acts as an excitatory amino acid at glutamate receptors, inducing an agitated toxic delirium. Despite the name *Amanita muscaria*, muscarinic/anticholinergic effects are actually minimal, except for notable reddening of the skin. Described by some as similar to alcohol intoxication, these mushrooms can also induce powerful hallucinations and illusions, slurred incoherent speech, seizure, severe nausea and vomiting, transient deep sleep or coma, and headache that may persist for weeks (http://www.emedicine.com/ped/topic1505.htm). Misidentification is a serious risk because poisonous varieties typically grow in close proximity to *Amanita muscaria* and *Amanita pantherina*; *Amanita phalloides* (death cap) is especially lethal. Reactions to muscimol are estimated to be at 6 mg for muscimol and 30–60 mg for ibotenic acid; 100 g of dried *Amanita muscaria* has 180 mg of these compounds, of which only 25 mg may be ibotenic acid. Intoxication commences within 30 min of ingestion and peaks over the next 2–3 hr (Waser, 1979). Ibotenic acid apparently decarboxylates to form muscimol when drying the mushrooms and, after ingestion, is mostly excreted unmetabolized into the urine. This finding, unique perhaps

to these mushrooms, explains how intoxication sometimes occurred through reserving and drinking the urine of an individual who initially had consumed the mushrooms (Wasson, 1979). Shamanic practices with *Amanita muscaria* have been noted with traditional peoples of the Arctic Circle and also by some Native American tribes, as well. These mushrooms grow throughout much of the United States but poison control centers rarely, if ever, are contacted about suspected *Amanita* spp. poisonings.

10. Special legal issue: When sacramental religious use is permitted

While sacramental peyote use in the United States is federally sanctioned only for native members of the NAC, the Santo Daime and UDV have no racial or ethnic exclusionary rules and are open to peoples of any background much like any church in America. The governments of Peru and Brazil have for more than 20 years recognized these faiths as bona fide religions that venerate the preparation and ingestion of ayahuasca. The Santo Daime and UDV have also quietly expanded into Europe, the United States, and elsewhere. A 2001 court case in the Netherlands also led to recognition of the Santo Daime as a valid religion; religious use of ayahuasca might now be legally permissible in all nations comprising the European Union (http://www.santodaime.org/community/news/0506_holland.htm).

The legal status of sacramental ayahuasca in the United States is now in federal litigation, with the American branch of the UDV seeking protection from interference with their religious practices by the US Department of Justice and, more specifically, the DEA. Members of religions such as the UDV and Santo Daime risk prosecution for the possession and distribution of their sacrament because it contains DMT, a Schedule I drug. Not surprisingly, the government does not wish to consider that for some Americans such enforcement amounts to religious persecution. Yet at the federal district and appellate levels, the UDV has achieved a preliminary injunction barring the US Department of Justice from enforcing drug laws against the UDV and calling on the government to enter into negotiations on how to regulate ayahuasca to ensure it is not diverted for illicit purposes. Unyielding in its assertion that no reasonable accommodation can be made to protect the religious freedoms of the UDV, the US Department of Justice's appeal has been accepted for another review, now before the full 10th Circuit Court of Appeals. Should the UDV continue to prevail in federal courts, the United States would be poised to have to accept a religion that uses a hallucinogen as its sacrament and that is open to all citizens for potential membership. Already, in November, 2000, the State of Oregon's Board of Pharmacy issued to the Santo Daime a religious exemption from state narcotics control for sacramental ayahuasca, offering the opinion that, "the sacramental use of the Santo Daime tea in the context of a bona fide religious ceremony by practitioners of the Santo Daime religion as described does not constitute abuse of a controlled substance."

Turning to the legal status issues surrounding peyote, as mentioned, under federal law, the United States denies the possibility that anyone other than Native Americans could have genuine religious need for the ingestion of peyote. A few states do not make any racial or ethnic distinctions, but only Native Americans who have tribal membership recognized by the Bureau of Indian Affairs have clear exemption from federal laws dealing with possession and distribution of peyote, provided the peyote is for traditional use such as for the NAC. The regulations governing this special status have "gray" areas over issues such as the transportation of peyote by First Nation peoples of Canada through the United States, issues over native blood quanta for purchase of peyote in Texas (25%) versus elsewhere (not defined), use of peyote by state-recognized tribes that do not have federal status, and the use of peyote by specially invited nonnatives, such as those who are married to Native Americans. In general, these issues "take care of themselves" because peyote has never been a major drug of abuse and the NAC has a long and positive history of cooperation with the DEA. Moreover, whenever a court case involves peyote, it is closely followed by the NAC as these Native Americans are proactive in ensuring that their hard-won rights are not threatened by illegitimate/illegal activity.

While these rules have, as mentioned, worked quite well for the NAC for decades, the DEA began to redraft these regulations in 2000 by deleting all mention of the NAC. Purportedly, this was done to bring the wording in line with the 1994 Amendments of the American Indian Religious Freedom Act, which explicitly affords federal protection to Native Americans who traditionally and ceremonially use peyote and other items considered sacred (e.g., eagle feathers). The DEA revisions concerning peyote were no doubt also motivated by the desire to prevent groups like the UDV from claiming that if the NAC has exemption for their psychoactive sacrament then under the equal protection clause of the Constitution they, too, should be exempt. To date, no such claim has ever succeeded in federal court because this protection to Native Americans is not based on freedom of religion issues but rather on the federal government's obligation by treaty to uphold and protect in perpetuity the traditions and customs of these peoples who have recognized limited sovereignty.

Regrettably, removing from the regulations any mention of the need for membership in the NAC has had the unintended consequence of delegitimizing use of peyote by those who fall within the longstanding "gray" zones mentioned above. While such use had been decided within the NAC on a case-by-case basis for decades and without problem, the DEA's "need" for such an overly precise definition in some instances has split apart native families across racial lines. While it is understandable that such "self-policing" is motivated by respect for law and to

ensure continued full protection of NAC access to peyote, some members apparently have yet to recognize that their private deliberations over invitations to nonmembers and to special cases have been co-opted by these new DEA rules; no other legally recognized religious faith in this country is subject to such government intrusion.

11. Summary and conclusions

Psychoactive drugs that are powerfully intoxicating hallucinogens and dissociative agents do not just originate from clandestine labs and an illicit drug distribution system; in the United States, many such substances can be located growing wild or in gardens, although often unrecognized. Accidental ingestion, misidentification, inadequate respect for safety, and overdose do result in emergency room visits, sometimes with serious morbidity and mortality.

Other than the ongoing popular use of psilocybin-containing mushrooms, the illicit, recreational use of the psychoactive botanicals reviewed in this article is quite minimal in comparison to abuse of well-known substances, such as cocaine or the opiates. *Salvia divinorum* has increased in use, however, illustrating how a shamanic tool can become harmful when ingested outside of any cultural context or proper preparation. Currently unregulated, awareness of *Salvia divinorum* has expanded due to the transmission of information and the availability of plant products via the Internet as well as sensationalistic news coverage by traditional media outlets. It is important to recognize that the emergence of *Salvia divinorum* into popular awareness, however, could repeat itself with these other botanicals (Lohrer & Kaiser, 1999). Younger patients and others who "surf" the Internet should at least be questioned by their physicians about what sort of information they are obtaining online about drugs.

Drug education should also expand to caution better about these indigenous botanicals, taking into account the special issues of those Americans who partake of a psychoactive sacrament as the central expression of their genuine religious faith. As history has proven with the NAC, the threat to public welfare does not emanate from religious practice but from individuals engaging in irresponsible, illicit drug abuse. Although peyote is a Schedule I illicit substance, the 300,000 Native Americans of the NAC are permitted the "nondrug, sacramental use" of peyote. Such accommodations may expand to American members of the UDV and Santo Daime for their "nondrug, sacramental use" of ayahuasca. Although virtually all of the plants reviewed in this article have ties to ancient shamanism and some continue to possess important religious and ceremonial significance, it is impossible to prevent determined individuals from seeking out these plants for other purposes. The quick ease with which a reader might identify one of these representative drugs growing in nature should also reinforce the need for further engagement with patients and the public about possible use of drugs from botanical sources.

References

Agurell, S. (1969). Cactaceae alkaloids I. *Lloydia 32*, 206–216.

Al Assmar, S. E. (1999). The seeds of the Hawaiian baby woodrose are a powerful hallucinogen. *Arch Intern Med 159*, 2090.

Ardila, A., & Moreno, C. (1991). Scopolamine intoxication as a model of transient global amnesia. *Brain Cogn 15*, 236–245.

Arnett, A. (1995). Jimson weed poisoning. *Clin Toxicol Rev 18*, 1–2.

Arora, D. (1990). *Mushrooms Demystified: A Comprehensive Guide to the Fleshy Fungi*. Berkeley, CA: Ten Speed Press.

Barker, R. E., & Hovin, A. W. (1974). Inheritance of indole alkaloids in reed canary grass (*Phalaris arundinacea* L.): I. Heritability estimates for alkaloid concentration. *Crop Sci 14*, 50–53.

Baxter, C., & Slaytor, M. (1972). Biosynthesis and turnover of *N,N*-dimethyltryptamine and 5-methoxy-*N,N*-dimethyltryptamine in *Phalaris tuberosa*. *Phytochemistry 11*, 2767–2773.

Borsutzky, M., Passie, T., Paetzold, W., Emrich, H. M., & Schneider, U. (2002). Hawaiian baby woodrose: (Psycho-)pharmacological effects of the seeds of *Argyreia nervosa*. A case-orientated demonstration. *Nervenarzt 73*, 892–896.

Brown, J. H., & Taylor, P. (2001). Muscarinic receptor agonists and antagonists. In: J. G. Hardman, L. E. Limbird, & A. G. Gilman (Eds.), *Goodman and Gillman's The Pharmacologic Basis of Therapeutics* (pp. 155–174). New York: McGraw-Hill.

Callaway, J. C., Raymon, L. P., Hearn, W. L., McKenna, D. J., Grob, C. S., Brito, G. S., & Mash, D. C. (1996). Quantitation of *N,N*-dimethyltryptamine and harmala alkaloids in human plasma after oral dosing with ayahuasca. *J Anal Toxicol 20*, 492–497.

Carlini, E. A. (2003). Plants and the central nervous system. *Pharmacol Biochem Behav 75*, 501–512.

Chao, J. M., & Der Marderosian, A. H. (1973). Ergoline alkaloidal constituents of Hawaiian baby wood rose, *Argyreia nervosa* (Burm. f.) Bojer. *J Pharm Sci 62*, 588–591.

Crosby, D., & McLaughlin, J. (1973). Cactus alkaloids: XIX. Crystallization of mescaline HCl and 3-methoxytyramine HCl from *Trichocereus pachanoi*. *Lloydia 36*, 416–418.

de Rios, M. D., Grob, C. S., & Baker, J. R. (2002). Hallucinogens and redemption. *J Psychoact Drugs 34*, 239–248.

Grella, B., Dukat, M., Young, R., Teitler, M., Herrick-Davis, K., Gauthier, C. B., & Glennon, R. A. (1998). Investigation of hallucinogenic and related beta-carbolines. *Drug Alcohol Depend 50*, 99–107.

Grinspoon, L., & Bakalar, J. B. (1997). *Psychedelic Drugs Reconsidered*. New York: The Lindesmith Center.

Grob, C. S., McKenna, D. J., Callaway, J. C., Brito, G. S., Neves, E. S., Oberlaender, G., Saide, O. L., Labigalini, E., Tacla, C., Miranda, C. T., Strassman, R. J., & Boone, K. B. (1996). Human psychopharmacology of hoasca, a plant hallucinogen used in ritual context in Brazil. *J Nerv Ment Dis 184*, 86–98.

Halpern, J. H. (1996). The use of hallucinogens in the treatment of addiction. *Addict Res 4*, 177–189.

Halpern, J. H., & Pope, H. G. (2001). Hallucinogens on the Internet: a vast

new source of underground drug information. *Am J Psychiatry 15*, 481–483.

Hashimoto, H., Clyde, V. J., & Parko, K. L. (1998). Botulism from peyote. *N Engl J Med 339*, 203–204.

Helmlin, H. J., & Brenneisen, R. (1992). Determination of psychotropic phenylalkylamine derivatives in biological matrices by high-performance liquid chromatography with photodiode-array detection. *J Chromatogr 593*, 87–94.

Hoffer, A., & Osmond, H. (1968). *New Hope for Alcoholics*. New Hyde Park, NY: University Books.

Isbell, H., Wolbach, A. B., Wikler, A., & Miner, E. J. (1961). Cross tolerance between LSD and psilocybin. *Psychopharmacologia 2*, 147–159.

Johnston, L. D., O'Malley, P. M., & Bachman, J. G. (2003). *Monitoring the Future National Results on Adolescent Drug Use: Overview of Key Findings, 2002*. Bethesda, MD: National Institute on Drug Abuse.

Kapadia, G. J., & Fayez, M. B. (1973). The chemistry of peyote alkaloids. *Lloydia 36*, 9–35.

Kluckhohn, C. (1944). *Navaho Witchcraft*. Boston, MA: Beacon Press.

Lindenblatt, H., Kraemer, E., Holzmann-Erens, P., Gouzoulis-Mayfrank, E., & Kovar, K. A. (1998). Quantitation of psilocin in human plasma by high-performance liquid chromatography and electrochemical detection: comparison of liquid-liquid extraction with automated on-line solid-phase extraction. *J Chromatogr B Biomed Sci Appl 709*, 255–263.

Lohrer, F., & Kaiser, R. (1999). Biological hallucinogens. New patterns of substance abuse in young addicts? *Nervenarzt 70*, 1029–1033.

Mack, J. P. G., Mulvena, D. P., & Slaytor, M. (1988). *N,N*-Dimethyltryptamine production in *Phalaris aquatica* seedlings: a mathematical model for its synthesis. *Plant Physiol 88*, 315–320.

McKenna, D. J., Towers, G. H., & Abbott, F. (1984). Monoamine oxidase inhibitors in South American hallucinogenic plants: tryptamine and beta-carboline constituents of ayahuasca. *J Ethnopharmacol 10*, 195–223.

Miller, M. D. (1970). Isolation and identification of lysergic acid amide and isolysergic acid amide as the principal ergoline alkaloids in *Argyreia nervosa*, a tropical wood rose. *J AOAC 53*, 123–127.

Musshoff, F., Madea, B., & Beike, J. (2000). Hallucinogenic mushrooms on the German market—simple instructions for examination and identification. *Forensic Sci Int 113*, 389–395.

Naranjo, C. (1979). Psychotropic properties of the harmala alkaloids. In: D. H. Efron, B. Holmstedt, & N. S. Kline (Eds.), *Ethnopharmacologic Search for Psychoactive Drugs vol. 1645*, (pp. 385–391). Washington, DC: U.S. Public Health Service Publication.

National Drug Intelligence Center. (2003). Information bulletin: *Salvia divinorum*. *Microgram XXXVI*, 122–125.

Pardanani, J., McLaughlin, J., Kondrat, R., & Cooks, R. (1977). Cactus alkaloids: XXXVI. Mescaline and related compounds from *Trichocereus peruvianus*. *Lloydia 40*, 585–590.

Pennes, H. H., & Hoch, P. H. (1957). Psychotomimetics, clinical and theoretical considerations: harmine, WIN-2299 and nalline. *Am J Psychiatry 113*, 887–892.

Petroski, R. J., Powell, R. G., & Clay, K. (1992). Alkaloids of *Stipa robusta* (sleepygrass) infected with an *Acremonium* endophyte. *Nat Toxins 1*, 84–88.

Riba, J., Anderer, P., Morte, A., Urbano, G., Jane, F., Saletu, B., & Barbanoj, M. J. (2002a). Topographic pharmaco-EEG mapping of the effects of the South American psychoactive beverage ayahuasca in healthy volunteers. *Br J Clin Pharmacol 53*, 613–628.

Riba, J., Rodriguez-Fornells, A., & Barbanoj, M. J. (2002b). Effects of ayahuasca on sensory and sensorimotor gating in humans as measured by P50 suppression and prepulse inhibition of the startle reflex, respectively. *Psychopharmacology (Berl) 165*, 18–28.

Riba, J., Rodriguez-Fornells, A., Urbano, G., Morte, A., Antonijoan, R., Montero, M., Callaway, J. C., & Barbanoj, M. J. (2001). Subjective effects and tolerability of the South American psychoactive beverage ayahuasca in healthy volunteers. *Psychopharmacology (Berl) 154*, 85–95.

Riba, J., Valle, M., Urbano, G., Yritia, M., Morte, A., & Barbanoj, M. J. (2003). Human pharmacology of ayahuasca: subjective and cardiovascular effects, monoamine metabolite excretion and pharmacokinetics. *J Pharmacol Exp Ther 306*, 73–83.

Rivier, L., & Lindgren, J. E. (1972). Ayahuasca, the South American hallucinogenic drink: an ethnobotanical and chemical investigation. *Econ Bot 29*, 101–129.

Roth, B. L., Baner, K., Westkaemper, R., Siebert, D., Rice, K. C., Steinberg, S., Ernsberger, P., & Rothman, R. B. (2002). Salvinorin A: a potent naturally occurring nonnitrogenous κ opioid selective agonist. *Proc Natl Acad Sci USA 99*, 11934–11939.

Schultes, R. E. (1969). Hallucinogens of plant origin. *Science 163*, 245–254.

Schultes, R. E., & Hofmann, A. (1980). *The Botany and Chemistry of Hallucinogens*. Springfield, IL: Charles C. Thomas.

Schultes, R. E., & Hofmann, A. (1992). *Plants of the Gods: Their Sacred, Healing and Hallucinogenic Powers*. Rochester, VT: Healing Arts Press.

Shulgin, A., & Shulgin, A. (1997). *TIHKAL: The Continuation*. Berkeley, CA: Transform Press.

Siebert, D. (1994). *Salvia divinorum* and salvinorin A: new pharmacologic findings. *J Ethnopharmacol 43*, 53–56.

Slotkin, T. A., DiStefano, V., & Au, W. Y. W. (1970). Blood levels and urinary excretion of harmine and its metabolites in man and rats. *J Pharmacol Exp Ther 173*, 26–30.

Stamets, P. (1996). *Psilocybin Mushrooms of the World: An Identification Guide*. Berkeley, CA: Ten Speed Press.

Stewart, O. (1987). *Peyote Religion: A History*. Tulsa, OK: University of Oklahoma Press.

Strassman, R. J. (1996). Human psychopharmacology of *N,N*-dimethyltryptamine. *Behav Brain Res 73*, 121–124.

Strassman, R. J. (2001). *DMT: The Spirit Molecule*. Rochester, VT: Park Street Press.

Thompson, A. C., Nicollier, G. F., & Pope, D. F. (1987). Indolealkylamines of *Desmanthus illinoensis* and their growth inhibition activity. *J Agric Food Chem 35*, 361–365.

Turner, D. M. (1994). *The Essential Psychedelic Guide*. San Francisco, CA: Panther Press.

USDA, NRCS, (2004). *The PLANTS Database (3.5)*. Baton Rouge, LA: National Plant Data Center.

Valdes, L. J., Diaz, J., & Paul, A. (1983). Ethnopharmacology of Ska Maria Pastora (*Salvia divinorum*, Epling and Jativa-M.). *J Ethnopharmacol 7*, 287–312.

Waser, F. G. (1979). The pharmacology of *Amanita muscaria*. In: D. H. Efron, B. Holmstedt, & N. S. Kline (Eds.), *Ethnopharmacologic Search for Psychoactive Drugs vol. 1645*, (pp. 419–439). Washington, DC: U.S. Public Health Service Publication.

Wasson, R. G. (1961). The hallucinogenic fungi of Mexico: an inquiry into the origins of the religious idea among primitive peoples. *Bot Mus Leaf, Harv Univ 19*, 137–162.

Wasson, R. G. (1962). A new Mexican psychotropic drug from the mint family. *Bot Mus Leaf, Harv Univ 20*, 77–84.

Wasson, R. G. (1979). Fly Agaric and Man. In: D. H. Efron, B. Holmstedt, & N. S. Kline (Eds.), *Ethnopharmacologic Search for Psychoactive Drugs. U.S. Public Health Service Publication, No. 1645*, (pp. 405–414). Washington, DC: U.S. Public Health Service.