# *Salvia divinorum*, Hallucinogens, and the Determination of Medical Utility

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## **Federal Drug Regulation**

During the eighteenth and nineteenths centuries, the United States Federal Government did not have any legislation that affected domestic drug use. During this time period, the regulation of drugs was delegated to state and local governments (Courtwright 2004; Friedman 1994; Musto 1999; Spillane 2000, 2004). In such an environment, drug use was common and widely unregulated. Brecher and the Editors of Consumer Reports (1972) referred to nineteenth-century America as a "dope fiend's paradise" (p. 3). Drugs such as opiates, cocaine, and marijuana were widely available through a variety of sources. Furthermore, a prescription from a licensed physician was not necessary to obtain drugs (Brecher and the Editors of Consumer Reports 1972; Courtwright 1982, 2001; Gahlinger 2004; Goode 2011; Musto 1999; Spillane 2000, 2004). Perhaps the most notorious example of the lack of regulation of drugs and the wide availability of them was the patent medicine industry. Pharmaceutical companies marketed and sold "patent" medicines: drugs that promised to cure virtually any and all ailments a person might be afflicted with (Courtwright 1982, 2001; Friedman 1994; Gahlinger 2004; Goode 2011; Hawthorne 2005; Musto 1999; Spillane 2000, 2004). These "medications" were referred to as "patent" medicines so that the manufacturers of these products did not have to disclose the formulas (Fischelis 1938).

In 1906, the Pure Food and Drug Act was passed. The law did not ban or control any drugs; it only required that makers of food products and drugs list the ingredients of their products (Friedman 1994; Gahlinger 2004; Goode 2011; Musto 1999; Spillane 2000, 2004). Passage of the legislation was the culmination of many years of intense lobbying efforts. As Sutherland (1940) noted, 140 pure food and drug bills were introduced in Congress over a 30-year period before the Pure Food and

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Drug Act was finally passed. Sutherland attributed the delay in the passage of the legislation to the strenuous lobbying efforts of the pharmaceutical industry. Only 8 years later, in 1914, Congress passed the Harrison Narcotic Act. The act was largely intended as a record-keeping law to track sales of opiates and cocaine, but it also required a prescription by a physician before these drugs could be dispensed (Acker 2002; Courtwright 1982; Gahlinger 2004; Musto 1999; Spillane 2000, 2004). Not only did the Harrison Narcotic Act limit who could dispense drugs. but the act also limited who could be considered legitimate patients. Prior to passage of the Harrison Narcotic Act, many physicians would prescribe controlled dosages of opiates to addicts, a practice referred to as "addiction maintenance." This was considered an acceptable practice of medicine. However, the Harrison Narcotic Act required that all drugs be "prescribed in good faith." The United States Supreme Court interpreted this clause as a prohibition against the dispensation of drugs to addicts. Thus, a sizable population of "patients" became "criminals" if they decided to continue taking drugs because they could no longer legally obtain them from a physician (Acker 2002; Courtwright 2001; Goode 2011; Musto 1999; Spillane 2000, 2004). The Harrison Narcotic Act and the subsequent Supreme Court decisions that disallowed addiction maintenance firmly established medical utility as one of the deciding criteria to determine if a drug should be available to the public. Additionally, final authority to determine if a drug has medical utility would be vested within the government.

Although marijuana was not included in the Harrison Narcotic Act, marijuana would later be controlled through separate legislation (Bonnie and Whitebread 1999; Gahlinger 2004; Goode 2011; Himmelstein 1983; Musto 1999). The first marijuana prohibitions began at the state level when Massachusetts prohibited the sale of marijuana without a prescription in 1914. Several other states passed similar legislation and by 1933, 29 states prohibited the non-medical use of marijuana (Bonnie and Whitebread 1999). In 1937, the United States federal government passed the Marihuana Tax Act. The legislation required people registered with the federal government to pay a \$1.00 per ounce tax every time marijuana was transferred between people. If a person was not registered with the federal government, the tax was \$100.00 per ounce (Bonnie and Whitebread 1999; Gahlinger 2004; Goode 2011; Musto 1999). According to Bonnie and Whitebread (1999), federal lawmakers did not want to add marijuana to the Harrison Narcotic Act because they feared that inclusion within the act would indicate that marijuana had recognized medicinal properties. Thus, federal lawmakers decided to develop a prohibitive regulatory tax based upon the National Firearms Act, which required a \$200 tax on every machine gun that was sold. (For more information about case law concerning marijuana, please consult the chapter by Brown in this book.)

Although the Harrison Narcotic Act controlled the medical use of opiates and cocaine and the Marihuana Tax Act effectively made marijuana illegal (unless someone could afford to pay the prohibitive tax), it quickly became clear that the United States federal government needed a new strategy to effectively regulate drugs. New drugs were rapidly emerging, many of which were not opiates. Thus, the Harrison Narcotic Act would have to be continually amended or, perhaps, a new

regulatory process was needed. Two categories of drugs would be the driving force behind the next federal legislative attempt at more efficient regulation: amphetamines and barbiturates (Rasmussen 2008; Spillane 2004). In 1965, the United States passed the Drug Abuse Control Amendments (DACA). DACA regulated and required physician's prescriptions for three categories of drugs: barbiturates, amphetamines, and central nervous system (CNS) stimulants. The legislation also added in another catchall category of drugs with a "potential for abuse" due to any depressant, stimulant, or hallucinatory effect. This last catchall category was developed for two purposes. The first purpose was that federal drug regulators recognized the need to plan ahead for the regulation of future drugs. The second purpose was the negative reputation lysergic acid diethylamide (LSD) was gaining (Spillane 2004). LSD was first synthesized in 1938 by chemist Alfred Hoffman while working for the Sandoz pharmaceutical company. Hoffman did not realize the psychoactive properties of LSD until he accidentally spilled a small amount of the drug on his hand in 1943. Four years later, Sandoz introduced LSD to the pharmaceutical market under the trade name Delysid. Psychiatrists and the United States military were among the first to research the possible applications of LSD (Gahlinger 2004; Lee and Shlain 1994). By the mid-1960s, 2,000 scientific articles had been published discussing the drug (Gahlinger 2004). However, primarily due to the actions of Harvard psychology professors Timothy Leary and Richard Alpert, who began as researchers studying the potential therapeutic benefits of the drug but primarily became known as advocates of the recreational use of LSD, the drug gained a notorious reputation and was thoroughly demonized (Gahlinger 2004; Griffiths and Grob 2010; Hofmann 2005; Johnson et al. 2008; Lee and Shlain 1994). Although DACA represented a step in the direction towards developing a more efficient regulatory framework for the regulation of drugs, it had several shortcomings. The most prominent of these shortcomings was that the legislation did not differentiate between regulated drugs. As Spillane (2004) notes, "Pharmaceutical manufacturers who may have been willing to accept some measure of additional regulatory control over their products resisted being lumped together with other drugs they regarded as obviously more dangerous" (p. 21). DACA was short-lived and would only last for 5 years until the current regulatory framework was enacted.

In 1970, the United States federal government enacted the CSA as Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970. The CSA replaced all existing federal legislation that regulated drugs. Although the CSA is multi-faceted and regulates several other aspects of drug use, the most important part of the CSA is the classification system for drugs it established, or as it is known within the act, the scheduling process. Five categories or "schedules" of drugs are established based upon eight criteria, three of which seem to be the most important: medical utility, safety of the drug, and potential for abuse. Schedule I, the most restrictive classification within the CSA, is reserved for drugs with no recognized medical utility, a very high likelihood of abuse, and some degree of danger (Courtwright 2004; Gahlinger 2004; Goode 2011; Griffin et al. 2008; Spillane 2004). Examples of Schedule I drugs are: gamma hydroxybutyrate acid (GHB),

diacetylmorphine (heroin), LSD, marijuana, and methylene-dioxy-methamphetamine (MDMA). As Jaffe (1985) notes, the process of scheduling has greatly affected the practice of medicine and biomedical research. The consequences of the process have proven both beneficial and costly. Although the system provides a mechanism through which the abuse liability of drugs can be more comprehensively considered, restrictive scheduling can effectively remove drugs from a physician's available options for the treatment of patients and place rigid restrictions on researchers that can effectively prevent research. For instance, during her testimony before the United States House Commerce Committee, Engel (1999) of Orphan Medical recounted the hurdles her company would face if GHB was placed into Schedule I. To comply with security protocols required for research utilizing a Schedule I drug, she speculated her company would have to build a \$20 million dollar facility.

Perhaps more controversial than the fiscal hurdles required to conduct research using Schedule I drugs is who has the power to decide if a drug has medical utility. Although the FDA provides recommendations for the proposed schedule a drug should be classified within, ultimate scheduling authority resides in the Drug Enforcement Administration (DEA), unless overridden by congressional legislation. On July 27, 1984, the DEA announced the agency intended to classify MDMA as a Schedule I drug. Several drug researchers and medical practitioners protested the decision and, as a result, hearings were scheduled to review the decision. After the DEA conducted hearings in Washington, DC, Kansas City, and Los Angeles, the DEA determined that Schedule I was an appropriate classification for MDMA. Supporters of MDMA were not deterred by the decision and eventually the matter was litigated in court. Both an administrative law judge and the First District Court of Appeals disagreed with the DEA and ruled that MDMA should be placed into Schedule III. However, the DEA was only required to reconsider their decision administratively. On March 23, 1988, MDMA was once again classified as a Schedule I substance, where it has remained since (Eisner 1994).

Debates concerning the medical utility of drugs such as marijuana, MDMA, GHB, and others that have been classified as Schedule I, usually concern some amalgamation of the utility and the socially constructed reputation of the substance itself. However, the class of drugs known as the hallucinogens presents a much deeper debate. As many have noted, hallucinogens are often niche drugs with essentially no potential for abuse, addiction or overdose. Many people find the psychoactive properties and altered states of consciousness caused by hallucinogens unpleasant. Some people will even describe these experiences as terrifying. Furthermore, this reputation alone may deter many from even trying hallucinogens. Indeed, the fact that so many hallucinogens are listed in Schedule I is more a testament to the negative reputation these drugs have been labeled with, primarily as a result of their constant association with the American counterculture movement of the 1960s (Gahlinger 2004; Goode 2011). Aside from these issues is a deeper comprehensive controversy that has existed since the Columbian Exchange: What should be considered an acceptable practice of medicine? Salvia divinorum, a plant with psychoactive properties that has recently gained attention within the popular media, and the scrutiny of lawmakers in many countries, including the United States, is another example of the complexities involved when considering hallucinogens.

### Salvia divinorum

*S. divinorum* is a member of the mint family. The active chemical within the plant, which is responsible for the psychoactive properties, is salvinorin A. This chemical has a unique effect on Kappa-opioid receptors, and the selective activation of the receptors typically results in an intense, but brief, dissociative state which typically lasts approximately 15 min or less (Grundmann et al. 2007; Prisinzano 2005; Roth et al. 2002; Siebert 1994). *S. divinorum* is native to the Oaxaca region of southern Mexico, a region inhabited by a group of indigenous people known as the Mazatecs (Wasson 1962). Gordon Wasson, a wealthy banker, was fascinated by psychoactive mushrooms and hallucinogens (Gahlinger 2004; Hofmann 2005). He financed many expeditions throughout the world to document different psychoactive mushrooms and plants, and was often accompanied by Harvard botanist Richard Schultes (Gahlinger 2004). Wasson embarked upon his first journey to Oaxaca in 1953 (Hofmann 2005; Wasson 1962).

Wasson (1962) noted "At an early date, we learned of a psychotropic plant that the Mazatecs consume when mushrooms are not available" (p. 77). Since Wasson was preoccupied with studying and documenting mushrooms, it was not until later that he investigated the plant he referred to as "a less desirable substitute" (p. 77). Eventually, Wasson obtained samples of the plant and submitted them to the Botanical Institute at Harvard University (Hofmann 2005). Due to the samples decaying in transit to the laboratory, it took several attempts before the plant could be identified (Wasson 1962). Eventually, botanists Carl Epling and Carlos Jativa identified the plant as a previously undiscovered (to the scientific community) species of salvia (Hofmann 2005). Wasson (1962) recounted that despite his friendly relations with the Mazatecs, and that they would freely discuss S. divinorum, the Mazatecs were unwilling to show Wasson either the seeds of the plant or where the plants were cultivated. Wasson noted that "virtually all" Mazatecs were aware of S. divinorum and he speculated that most had their own supply of plants. He believed the plants were located in remote ravines, but Wasson and his companions never personally observed any places where S. divinorum was cultivated. This secretive practice surrounding the cultivation of hallucinogens dates back to the arrival of Spanish conquistadors to the Americas, who believed the use of hallucinogens were akin to pagan rites and the work of the devil. The Spanish attempted to prevent indigenous people from continuing these practices, but only succeeded in driving them underground (Schultes et al. 2001).

Perhaps the biggest reason why hallucinogens are not more widely accepted by Western medicine is the continuing divide between European and Ameridian views of healing. As Schultes et al. (2001) note, many people who have belief systems

based upon ancient traditions (not just in the Americas) have believed that hallucinogens are useful to contact the spirit world and, in some cases, leave this plane of existence. Hallucinogens gain their medicinal value for people of traditional populations due to their understanding of what causes illnesses. For traditional Amerindian populations, illness is often believed to be caused by some disconnect between a person and the spirit world. Therefore, to ascertain what is ailing the person, a shaman (or *curandero* in mestizo cultures), will utilize hallucinogens to contact the spirit world and obtain a diagnosis for the afflicted person. For Mazatecan rituals, this is how S. divinorum is utilized. According to Wasson (1962), the Mazatec people would refer to S. divinorum as hojas de la Pastora. which means "leaves of the Shepherdess." In some instances the plant would be referred to as hojas de Maria Pastora, which means "leaves of Mary the Shepherdess." Wasson believed this was a strange name for S. divinorum because he was unaware of any tradition within Christianity that referred to the Virgin Mary as a shepherdess. Wasson speculated that this might be an attempt by the Mazatecs to "sanctify" a ritual that is rooted in paganism. Wasson could not determine how long S. divinorum rituals had been taking place. He speculated that the practice most likely predated the arrival of the Spanish to the Americas, but noted only cryptic references existed among early Spanish writers of a plant which *possibly* could have been S. divinorum. Emboden (1979) states, that in addition to S. divinorum, the mint family has several psychoactive species. S. divinorum does not grow from seeds, but the reclining branches of the plant fall to the ground and eventually root. Emboden noted that the plant needed to be cultivated to grow and did not appear to be present in the wild. S. divinorum does not flower until it reaches seven or more feet in length. Emboden describes the leaves of the plant as "almost an iridescent green."

Based upon observations during his expeditions, Wasson (1962) described one detailed example of a Mazatecan shamanistic ritual that involved S. divinorum. If a person was suffering from an illness and the source of the affliction could not be ascertained, S. divinorum would be used in a ceremony to determine the cause of the illness. A curandero would obtain 50 leaves of the plant if a patient "does not take alcohol," and one hundred leaves "when he takes alcohol." The leaves of S. divinorum are "rubbed" in water and "the potion" is given to a patient in a quiet isolated place at midnight. After a patient has ingested S. divinorum, the curandero will wait 15 min for the drug to take effect. The patient will enter into a dissociative state and will speak "in a trance." The curandero will listen to the patient and presumably obtain a diagnosis for the illness. Eventually, the patient will shake their clothes to rid themselves of the evil spirits that are causing the illness. When day breaks, the curandero will prepare a bath for the patient using the water in which S. divinorum has been "rubbed" and bathe the patient. The Mazatecs believe that the bath will end the patient's dissociative state. Wasson also recounted that a S. divinorum ritual could be used to investigate claims of theft or when something is lost.

In addition to the route of administration Wasson (1962) described, Siebert (1994) notes that *S. divinorum* leaves can be chewed as well. He states that the leaves must be chewed thoroughly so that the salvinorin A can be absorbed by

the oral mucosa. Furthermore, the longer a person chews *S. divinorum* leaves, the greater the intensity of the dissociative state. If the leaves are swallowed too quickly, salvinorin A cannot produce intoxication because the body's digestive system will deactivate the chemical. Lastly, *S. divinorum* may be smoked. Leaves of the plant can be crushed and smoked or the leaves can be impregnated with tinctures of salvinorin A extract. Salvinorin A extract can be purchased in different levels of potency and is more powerful than smoking the unadulterated leaves (Gonzalez et al. 2006; Bucheler et al. 2005; Siebert 1994). Smoking *S. divinorum* appears to be the most common route of administration among recreational users (Khey et al. 2008; Miller et al. 2009; Stogner et al. 2012).

Siebert (1994) lists many different effects people have reported while under the influence of S. divinorum. In some cases, people perceived that they were inanimate objects. This is a phenomenon Kelly (2011) observed when he conducted qualitative interviews with 25 S. divinorum users. One of the survey participants recounted that on one occasion, when he was under the influence of the drug, "I thought I was made out of Legos" (p. 48). Another user reported that he felt as if he had been turned "into a piece of art on the wall and people were looking at me" (p. 48). Some people have reported a sense of déjà vu (Siebert 1994). Singh (2007) reported a case study of a 15-year old boy who, in addition to experiencing déjà vu, appeared paranoid, could not articulate his thoughts, and had slow speech for a three-day period of time after using Salvia. Siebert (1994) stated that some people lost the sense of their body and, in some cases, believed there were some unknown forces physically affecting their body. The use of S. divinorum has been known to cause uncontrollable laughter in many users. Lastly, Siebert noted that, while under the influence of the drug, some people reported overlapping realities or a sense that they were in different places at the same time. Kelly (2011) recounts one user, while under the influence of S. divinorum, felt as if he was transported to the "Spanish coast." One user reported that time seemed to stand still, while another reported his trip seemed much longer than it had actually been. One consistent finding among researchers, which Siebert (1994) recounts, is while some users of S. divinorum reported similar effects to other hallucinogens, such as ketamine or dimethyltryptamine (DMT), many have noted that S. divinorum provided a "quite unique" experience (Siebert 1994). One example of this type of experience was described in a television news report when a person who had used S. divinorum stated "In my personal opinion, it's like taking acid and mushrooms and ecstasy and slamming a 40 and huffing a nitrous balloon all at the same time" (Blake 2006). Some researchers have recognized S. divinorum as one of the most potent naturally occurring hallucinogens (Bucheler et al. 2005; Valdes 1994).

Exactly when recreational use of *S. divinorum* began is unknown. Halpern and Pope (2001) conducted an Internet search on December 10, 1998 by entering the word "hallucinogens" into the yahoo.com search engine. At that time, yahoo.com was the most commonly used Internet search engine. The researchers identified 81 websites from their search. Among the search results was a now-defunct website with the URL http://ethnobotany.com. Leaves of *S. divinorum* were available for purchase from this website. When describing the plant, Halpern and Pope referred

to it as "a plant containing the little-known hallucinogen salvinorin A" (p. 482). In February of 2004, Dennehy et al. (2005) conducted an Internet search using the search engines from google.com, vahoo.com, aol.com, and msn.com. The authors used two search terms: "buy herbal high" and "buy legal high." Ephedra alkaloids were the most commonly mentioned substance, mentioned in 27 % of the websites that were identified. However, as the researchers noted, these substances were removed from the market by order of the FDA on April 12, 2004. The second most commonly mentioned substance was S. divinorum, mentioned in 17 % of the websites that were identified. Although it could be argued whether this amount of information indicated S. divinorum was popular or could be considered a commonly available substance, as Griffin et al. (2008) noted, "one could surmise that S. divinorum products have taken the place of ephedra as the most common substance available via the Internet" (p. 184). They further note that the first "major" article to appear in the United States was published in *The New York* Times on July 9, 2001. Thus, it appears recreational use began at some point during this time period.

As Griffin et al. (2008) have noted, S. divinorum has received considerable attention in the media. Most of the attention has been based upon stories that a hallucinogenic drug is (or was) legally available. Among media accounts, three events seemed to have garnered the most attention. In January of 2006, a teenager in Delaware, Brett Chidester, committed suicide. After the suicide, police officers found S. divinorum in Brett's vehicle. No other drugs were found nor were any drugs detected in his system during autopsy. Brett's mother, Kathleen Chidester, believed S. divinorum use "reshaped" the mind of her son (Moran and Culhane 2007). After conducting an initial autopsy, the medical examiner later revised the cause of death to include S. divinorum as a contributing factor to the suicide. This action was partially based upon a reading of Brett's journal entries, which discussed the revelations he discovered after using S. divinorum. Brett stated that smoking the plant led him to the belief that there were "different dimensions of reality that left him with an empty feeling about this world" (Griffin et al. 2008, p. 188). Three months after his death, Delaware passed "Brett's Law," which classified S. divinorum as a Schedule I drug within the Delaware state controlled substances act (Griffin et al. 2008). In December of 2010, videos appeared on the website youtube.com of the musician and actress Miley Cyrus smoking S. divinorum. As Murphy et al. (2011) document, postings on twitter.com and Google searches spiked considerably after these videos were posted. Postings of videos of people smoking S. divinorum are not limited to Miley Cyrus, though; several researchers have documented the phenomenon of S. divinorum users posting videos of themselves while under the influence of the drug on youtube.com (Casselman and Heinrich 2011; Lange et al. 2010). In January of 2011, Jared Loughner shot Arizona Congresswoman Gabrielle Giffords (D-AZ) at a Tucson campaign event. After the shooting, the television program Nightline explored Loughner's use of S. divinorum as part of an investigation into the possible motives that led to the shooting. The report specifically mentioned his discussion of existential realities (Stogner et al. 2012).

Despite the considerable media attention on S. divinorum, so far, the United States federal government has declined to list the plant as a scheduled substance. In 2002, U.S. Representative Joe Baca introduced H.R. 5607, the Hallucinogen Control Act of 2002. If the law had passed, both S. divinorum and salvinorin A would have been classified as Schedule I drugs. However, the bill died in committee and new legislation has not been introduced. As Griffin et al. (2008) note, the federal inaction regarding S. divinorum is a relatively unique occurrence after the passage of the CSA. In the face of federal inaction, individual states have stepped in and taken a variety of approaches to regulate S. divinorum. According to Stogner et al. (2012), individual states that have chosen to regulate S. divinorum have chosen one of three strategies: classifying S. divinorum and/or salvinorin A as a Schedule I substance within state controlled substances acts, passing a separate law from state controlled substances acts which regulates S. divinorum and/or salvinorin A, or establishing an age limit for people who are allowed to purchase or possess S. divinorum and/or salvinorin A. In August of 2005, Louisiana was the first state to take action; enacting legislation that prohibited the production, manufacture, and distribution of several hallucinogenic plants, one of which was S. divinorum. Other states that have passed separate legislation regulating the plant are: Tennessee, North Carolina, West Virginia, and Wisconsin. Also in August of 2005, Missouri classified S. divinorum as a Schedule I substance. Since then, Delaware, Oklahoma, North Dakota, Florida, Illinois, Kansas, Mississippi, Virginia, Hawaii, Nebraska, Ohio, South Dakota, Alabama, Georgia, Kentucky, Michigan, Minnesota, Connecticut, Indiana, Pennsylvania, Wyoming, and Colorado have added S. divinorum to Schedule I of their state controlled substances acts as well. In 2007, Maine passed a law that prohibited people under the age of 18 from possession of S. divinorum. California restricts the sale of S. divinorum and salvinorin A to minors. Maryland prohibits the possession of S. divinorum and salvinorin A to people under the age of 21.

As Griffin et al. (2008) state, regulation of S. divinorum seems to be simply focused on the fact that a legal hallucinogen was available. There is no real evidence that the use of S. divinorum is either dangerous or widespread. The first published prevalence study of S. divinorum was conducted by Lange et al. (2008). The researchers surveyed 1,571 university students at a large public university in the southwestern United States during the fall semester of 2006 and the spring semester of 2007. They reported S. divinorum had been used by 4.4 % of the students within the past year. They further identified the most likely users to be White males, fraternity members, and heavy episodic drinkers; people they identified as most likely to engage in substance use generally. In that same year, Khey et al. (2008) published the results of a survey of 825 university students at a large public university in the state of Florida, collected during the fall semester of 2006 and the spring semester of 2007. Only 22.6 % of students had even heard of S. divinorum. Of the total sample of students, 6.7 % had reported lifetime use of S. divinorum and 3 % reported use within the last year. Similar to Lange et al. (2008), Khey et al. (2008) found that White males were the most likely students to report that they had used S. divinorum. Additionally, Khey et al. found most people who had used *S. divinorum* reported they would not use the drug a second time. In a follow-up study utilizing the same data, Miller et al. (2009) found that university students who reported heavy use of marijuana were among the most likely users of *S. divinorum*. *S. divinorum* appeared to be used as a legal substitute for marijuana, but users did not generally report that *S. divinorum* use was pleasurable or an adequate substitute.

On the website www.erowid.org, Baggott et al. (2010) added a hyperlink that stated "survey for people who have used Salvia divinorum" and collected responses from 520 people from July 24, 2003 to August 20, 2003 who chose to complete a 20 min survey; 500 were included in the results of their study (92.6 % were male). The survey found that the median number of times a respondent had used S. divinorum during their lifetime was six occasions. Among the motivations respondents cited for using S. divinorum (in order of rank) were: to explore altered consciousness, curiosity, spiritual or mystical reasons, personal growth or selfunderstanding, contemplation or meditation, relaxation or enjoyment, to get high, to increase enjoyment of other activities, and to help a mainly psychological problem. One hundred and twenty-nine participants reported positive mood effects that lasted more than 24 h; 60 of these participants reported S. divinorum had "antidepressant-like effects." Participants who reported positive effects were most likely to want to use S. divinorum again. Only three people of the total participants who were surveyed believed they were addicted or dependent upon S. divinorum, while six people reported strong cravings.

Wu et al. (2011) utilized data files from the 2006–2008 National Surveys on Drug Use and Health (NSDUH), a federally sponsored ongoing study that surveyed 166,453 people aged twelve and older concerning issues related to health and substance use. The researchers noted that questions about *S. divinorum* use are included in a section of the survey called "special drugs." They noted 0.7 % of respondents reported lifetime use of *S. divinorum* in 2006. That percentage increased to 1.3 % in 2008. They found that use of *S. divinorum* was primarily associated with young adult White males who lived in large metropolitan areas. Among the reported users, many reported they had been arrested and many users reported they also suffered from depression. Additionally, respondents who reported *S. divinorum* use were commonly polydrug users. In a similar study utilizing the same data source, Perron et al. (2012) noted "salvia use is part of a broader constellation of psychosocial and behavioral problems among youth and young adults" (p. 1).

According to the literature that has investigated *S. divinorum*, it seems recreational use of the drug does not appear to be widespread and does not approach a level one could really even say is common. Much like other hallucinogens, *S. divinorum* appears to be a niche drug. Most of the people who have used *S. divinorum* do not use it again, and those who do seem to be people for whom drug use is relatively common and the use of *S. divinorum* is just one of the many drugs they might try. Additionally, there does not appear to be any real danger when *S. divinorum* is used. As Vohra et al. (2011) note, "A literature search in the PubMED database in December 2008 revealed no clinical case reports or case

series on the acute toxic effects of *S. divinorum*" (p. 643). They note over a 10-year period, from January 1998 to May 2008, 133 reports that mentioned salvia were reported to the California Poison Control System. Of these reports, 96 referred to various species of salvia plants that are not psychoactive and only 37 actually referred to *S. divinorum*. Additionally, only 18 reports referred to *S. divinorum* alone, the other 19 involved polydrug use. The only study that has indicated *S. divinorum* has any real abuse potential is Baggott et al. (2010). In that study, among 500 people who had used *S. divinorum*, only three users (0.6 %) reported they believed they were addicted and only six users (1.2 %) reported strong cravings for the drug. This is certainly underwhelming evidence of any real abuse liability.

The federal drug prohibitions of the recreational use of heroin and cocaine have existed for almost 100 years, but use still persists, despite what many consider draconian threats of punishments. Yet, the results of one study seem to indicate that the use of S. divinorum is more elastic. Stogner et al. (2012) surveyed 534 university students at the same university in Florida as Khey et al. (2008) after the State of Florida had classified S. divinorum as a Schedule I substance. Stogner et al. (2012) found that not one single student reported using S. divinorum in the previous year. Thus, it appeared that simply scheduling *S. divinorum* essentially eliminated use. This would tend to indicate that S. divinorum was not especially popular or desirable among drug users, making one wonder why the media seemed to fixate upon the little-used plant. Stogner et al. (2012) speculate that S. divinorum may very well have been just one of many recent drugs that the media will focus on before they get bored and move on to a new drug. Others have documented similar phenomena, such as Akers (1992) concept of the "scary drug of the year" and Jenkins (1999) concept of "synthetic panic." Stogner et al. (2012) noted that synthetic marijuana and methylenedioxypyrovalerone (MDPV, more commonly known as "bath salts") quite possibly could be garnering the media attention once held by S. divinorum.

#### **Medical Utility of Hallucinogens**

The placement of *S. divinorum* into Schedule I in so many state-controlled substances acts raises a persistent question that has been debated about hallucinogens since the enactment of the CSA: Do hallucinogens have any medical utility? With *S. divinorum*, this question is not exactly clear. According to Wasson (1962) and Schultes et al. (2001), *S. divinorum* is used medicinally under the auspices of shamanism; a belief system Western and European views of medicine largely do not recognize. Siebert (2006), an advocate of *S. divinorum*, argues the plant should not be used simply for recreational purposes, and should only be used by people seeking enlightenment. Again, such use does not seem to satisfy Western or European views of medicine. Although it seems that *S. divinorum* will not be prescribed to patients, salvinorin A and the research applications of the active chemical do seem promising. Prisinzano (2005) argued that studies of salvinorin A might help develop non-addictive painkillers or aid science in developing a more complete picture of how the brain works. This could potentially contribute to research on Alzheimer's disease and other mental illnesses. Roth et al. (2002) specifically noted that salvinorin A could help researchers understand perceptual disorders caused by such conditions as schizophrenia, dementia, and bipolar disorder. Vortherms and Roth (2006) have stated that salvinorin A might potentially be used to treat depression, chronic pain, and kidney ailments.

That so many individual states have rushed to premature judgment and placed S. divinorum into Schedule I of their state-controlled substances act seems to be just the next chapter in the continuing story of hallucinogens. That the United States federal government has failed to take action on S. divinorum is probably much more of a testament to the belief that the plant does not pose a danger than evidence of a progressive view that might allow research on a hallucinogenic substance to commence without undue restrictions. The excesses of people such as Timothy Leary and Richard Alpert, combined with the placement of seemingly every hallucinogen into Schedule I of the CSA, essentially seemed to end research into hallucinogenic drugs. Recently, however, there has been a revitalization of hallucinogenic drug research, beginning with the research of DMT by Rick Strassman (Johnson et al. 2008). Strassman (1996) argues that clinical studies of hallucinogens are necessary "to provide insights into many basic brain-mind relationships" (p. 121). Studies of avahuasca have noted that the responsible use of this drink, which contains DMT, can improve a person's mental health (Grob et al. 1996; Callaway et al. 1999; Santos et al. 2007) and could possibly be used for the treatment of alcoholism and substance abuse (McKenna 2004). As Labate et al. (2012) note, two psychotherapeutic centers for the treatment of substance dependence currently operate in Brazil and Peru which utilize ayahuasca as a part of the rehabilitation process. Labate et al. note that, while the centers claim their programs are effective in treating substance dependence, independent researchers have not yet been verified these findings using a rigorous scientific method. Sheppard (1994) suggests that ibogaine could potentially be used for the treatment of opiate addicts. Research on psilocybin may lead to a deeper understanding of mystical experiences and deeper insights into pharmacological and brain mechanisms (Griffiths et al. 2006, 2011). Researchers hope that by studying psilocybin they can also arrive at a greater understanding of attitudes, mood, behavior (Griffiths et al. 2011), and personality (MacLean et al. 2011).

Perhaps the biggest irony surrounding medical utility, hallucinogens, and research is that what once discredited them, might help preserve them. In 1990, the United States Supreme Court ruled in the case *Employment Division v. Smith* that individual states were allowed to prohibit the sacramental use of peyote by Amerindians; no such exception to this type of use existed in the CSA. As Bullis (2008) notes, this led to the passage of the Religious Freedom Act of 1993. Written into the act was an exception that allowed members of the Native American Church to use peyote during sacramental rituals. This exception was later applied to members of the União do Vegetal (UDV) religion, who engage in the sacramental

use of ayahuasca. Members of the UDV have been allowed to consume the drink in the United States, as well as in other countries that recognize this as a legitimate religious practice (Bullis 2008; Labate and Feeney 2012). (For more information about the UDV case, please consult the chapter by Feeney and Labate 2014.) Thus, two different hallucinogens that have been used as part of shamanistic rituals, but shunned by Western and European thought and religious practice, are once again officially permitted. Perhaps this bodes well for the revitalization of hallucinogenic research and indicates that the overreaction to the excesses of previous generations will not continue to haunt researchers who want to investigate hallucinogens in a responsible manner.

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