Chapter 4
The Use of *Salvia divinorum* from a Mazatec Perspective

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> *Some say it is a sensual and tactile thing. Some say it's about temporality and dimensionality, that it's about time travel. Some say it's about the Root Energy Network or that it's about becoming a plant. This plant is the great secret of our tradition. Consciousness has to do with energy and light. It is really very simple; neither animals nor people have consciousness. It is plants that have consciousness: Animals get consciousness by eating plants*
> [Dale Pendell about *Salvia divinorum*, from his book *Pharmako/Poeia* (1995, p. 158)].

Abstract *Salvia divinorum* is a medicinal and psychoactive plant endemic to the Sierra Madre Oriental of Oaxaca, Mexico. The Mazatec people have been using the leaves for centuries in ceremonies for its psychoactive properties and as a treatment for arthritis and inflammation, gastrointestinal problems, headaches, and addictions, among other uses. The active principle of *Salvia divinorum*, the terpene salvinorin A, is a uniquely potent and highly selective kappa-opioid receptor agonist and, as such, has enormous potential for the development of valuable medications. Among them, the most promising include safe and nonaddictive analgesics, neuroprotectors, short-acting anesthetics that do not depress respiration, antidepressants, anti-inflammatories, medications for the treatment of addiction to stimulants and alcohol, and drugs to treat disorders characterized by alterations in perception. The Mazatec consider *Salvia divinorum* to be a very powerful plant spirit that should be treated with utmost respect, and the preparation for the ceremony requires a strict regimen. They chew the fresh leaves at night while chanting and praying. In the Western use, the dry leaves are potentiated in extracts to be smoked. A lack of information about the appropriate doses and other considerations while smoking the extracts could result in overwhelming

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experiences due to the high potency and fast onset of the substance. For the Mazatec, smoking the plant is not the preferred mode. How could we create a bridge between the two perspectives? In this chapter, I will try to clarify the best ways to use *Salvia divinorum* for medicinal, psychotherapeutic, and inner exploration purposes.

Natural History of *Salvia divinorum*

Of the more than 1000 species of salvia that exist in the world, none has evoked as much fascination and curiosity as *Salvia divinorum*. It is a perennial and hydrophyte plant belonging to the mint family (Lamiaceae). It has a square and hollow stem, with decumbent secondary stems that allow it to propagate vegetatively, rooting from the nodes and internodes, and can regrow from the ground from senescent stems. This mysterious herb that loves to hide in moist and shadowy places is endemic to the Sierra Madre Oriental of Oaxaca, Mexico. The Mazatec people, who have been using *S. divinorum* for its medicinal and psychoactive properties for hundreds of years, know the plant in their language as "ska pastora" [sic]. As the Mazatec language is a tonal one, the word "ska" (meaning herb or leaf) has been reproduced in the literature as it sounds. Nevertheless, it seems that a more appropriate form of writing herb in Mazatec, closest to the actual sound of the word, would be *xkà* (Carrera, 2011). The Mazatec also refer to this plant with names in Spanish like "hierba de María" (Mary's herb) or "hojas de la pastora" (shepherdess' leaves). The names are related to the Virgin Mary, who they believe is incarnated in the plant. The lack of an indigenous name and the fact that there were no shepherds in Mexico before the arrival of the Spaniards suggest that *S. divinorum* could be a postcolonial introduction or that the original name in Mazatec could have been modified by Christian influence (Ott, 1995).

During the 1930s, various anthropological expeditions toured the Mazatec Sierra, which led to the rediscovery of the use of hallucinogenic mushrooms in the remote hamlet of Huautla de Jiménez. The anthropologist Jean Basset Johnson, who was part of the expeditions, discovered that the Mazatec used the juice of the leaves of a plant called "hierba de María" for divination, in what constitutes the first academic report on the existence of *S. divinorum* (Johnson, 1939). Johnson also knew that the Mazatec employed "semillas de la Virgen" (seeds of the Virgin) in their ceremonies (Johnson, 1939), which were later identified as seeds of the plant ololiuhqui, or morning glory, *Turbina corymbosa*. These seeds contain ergine (LSA), an alkaloid similar in structure to lysergic acid diethylamide (LSD) (Hofmann & Tscherter, 1960). In 1945, the anthropologist Blas Pablo Reko mentioned the use by the Mazatec and the Cuicatec of a "divination leaf," which, in all likelihood, was *S. divinorum* (Reko, 1945). Seven years later, the anthropologist Robert J. Weitlaner reported the therapeutic and divinatory use among the Mazatec of Jalapa de Díaz of a potion made by rubbing in water between 50 and 100 leaves

of "hierba de María," the highest dose being used for alcohol addicts. In addition to curing, Weitlaner observed that the leaves were employed to guess where an animal or person had been lost or who had committed a robbery (Weitlaner, 1952). Finally, the Mexican biologist and botanist Arturo Gómez Pompa classified, for the first time, *S. divinorum* as belonging to the *Salvia* genus but could not make a complete identification due to the absence of flowering material (Gómez Pompa, 1957).

The first flowering specimens of *S. divinorum* were collected by Robert Gordon Wasson and Albert Hofmann (Wasson, 1962) and sent to the greatest *Salvia* genus expert at the time, Carl Epling, for identification. In the description (Epling & Játiva, 1962), *S. divinorum* was classified within the section Dusenostachys, whose specimens are mostly endemic to Southern and Central Mexico. However, in a study using a molecular phylogenetic approach by DNA sequencing conducted in 2010 (Jenks, Walker, & Kim, 2010), samples of *S. divinorum* and 52 other *Salvia* species were compared within the subgenus *Calosphace*, to which *S. divinorum* belongs. No evidence was found to include *S. divinorum* in the Dusenostachys section proposed by Epling and Játiva or to consider the plant a hybrid. Also, in the botanical classification performed by Epling and Játiva, the flowers of *S. divinorum* are described with blue chalice and corolla (they are violet), an error that has persisted in the literature, including in the *Hallucinogenic Plants* by Richard Evan Schultes, and in the first edition of *Narcotic Plants* by William Emboden, among others. The official description was corrected by Aaron S. Reisfield in 1993, who described thoroughly the parts of the plant and performed exhaustive fieldwork in the Mazatec Sierra (Reisfield, 1993). Although the exact origin of *S. divinorum* remains a mystery, the results of the 2010 phylogenetic study suggest that *Salvia venulosa*, a rare perennial plant native to a small region of the Colombian Andes, is the closest relative of *S. divinorum*. Thyme (*Thymus vulgaris*), common sage (*Salvia officinalis*), mint (*Mentha piperita*), and basil (*Ocimum basilicum*) are other relatives of *S. divinorum* in the plant kingdom.

The first specimens of living and flowering *S. divinorum* that came out of Mexico and constitute the common strain of the plant that has spread throughout the world were collected at the Mazatec Sierra by psychiatrist and ecologist Sterling Bunnell, who introduced them to the United States in 1962. Bunnell deposited one in the Herbarium of the University of California at Berkeley, grew others in his home, and propagated them among botanists and friends like the chemist Alexander Shulgin. Therefore, the most common variety of *S. divinorum* commercially distributed around the globe is the "Bunnell variety," not the "Wasson and Hofmann variety," which in fact doesn't exist, because the specimens that they collected were dried and pressed, remaining in Mexico (Siebert, 2003).

Until the 1980s, it was believed that the production of seeds was extremely rare and that they were practically unfeasible, so that the reproduction of the plant was exclusively vegetative or by cuttings. This belief was based on the fact that the Mazatec reproduce the plant by seeding cuttings, and in the first expeditions by the Sierra, no populations of *S. divinorum* were found growing wild. Although today it is known that this belief is incorrect, since several researchers in the world have successfully managed to germinate new plants from seeds (Hanna, 1999; Siebert, 1999), their production is certainly scarce, and they seem to have a low rate of

germination and survival. However, some Mazatec have stated that the plant does indeed grow wild in the Sierra and that these plants produce seed that can be planted to grow *S. divinorum* (Valdes, Hatfield, Koreeda, & Paul, 1987).

Traditional Use

From the articles published by the researchers who later visited the Mazatec Sierra and participated in ceremonies with *S. divinorum* (see the review of literature from Valdes, Diaz, & Paul, 1983), we know that the Mazatec use the plant, in addition to the aforementioned uses, as a treatment for arthritis and inflammation, headaches, and gastrointestinal problems, for the treatment of eliminatory dysfunctions, and for treating alcohol addiction. Also mentioned is the employment of the leaves for general relief or as a tonic for the sick, the anemic, or the dying. About its shamanic uses, we know from the early reports that *S. divinorum* is the initiation plant or training herb for the future healer (it is considered the plant that is easiest to handle, with the least psychoactive power), followed by the "seeds of the Virgin" (named *naxole natjaoná* in Mazatec) and, finally, by the management of hallucinogenic mushrooms.

During my own fieldwork conducted in the Mazatec Sierra, I have learned that the leaves are applied in poultices to treat insect bites, eczema, and fungi. My feminine informers also remarked that *S. divinorum* is a wonderful plant for women as a remedy for candidiasis and other vaginal diseases, cystitis, and menstrual cramps. I spent some months living with a family in a Mazatec town, in which the older son had become addicted to inhalants and cocaine. The father, a well-known healer, treated his son successfully using *S. divinorum* in ceremonies, as well as with the administration of fresh leaves on alternate days for 1 month.

For the treatment of internal ailments, the bitter juice of 40 leaves or more is drunk right before going to sleep, to avoid the strong psychedelic effects of such a high dose and to obtain the therapeutic benefits on physical problems. The users that I interviewed reported vivid dreams and a significant and lasting remission of symptoms of pain, bronchitis, fever, back contractures, water retention, and inflammation after the night of treatment. The Mazatec say that the plant is a female doctor that works within their bodies to restore their health. I knew also that it is employed for treating symptoms similar to what we call depression or low mood, by eating a small pair of fresh leaves in the morning (the leaves are always consumed in pairs, which represent the human element of man and woman, symbolizing the dual principle of creation and procreation). As we will see later in this chapter, all the medicinal applications of the Mazatec are well supported by recent pharmacological findings.

The way in which the Mazatec consume the leaves depends on their application. In the case of ceremonies, they are well chewed and swallowed, or the mixture of crushed leaves with water is drunk for a softer effect. The number of leaves given to the patient will depend on the physical constitution, previous experience, and the

nature of the problem to be treated. The healer and the patient must follow a strict diet by refraining from eating certain foods, drinking alcohol and cold beverages, avoiding certain situations like funerals, and not having sex for a period ranging from several days to several weeks. During the ceremonies, which last for 4 or 5 h and take place in front of an altar at night in complete darkness, chants and prayers are sung. The healer asks questions of the patient, who expresses aloud his or her discoveries about the problem that elicited the consult. The effects appear after 20 or 30 min and consist of feelings of well-being; a sensation of internal peace and calm that lasts for days after the ceremony; out-of-body experiences; physical sensations of floating and of being touched or twisted or massaged; becoming a plant; organic visions of nature elements, animals, and other people; auditory experiences (listening to a soft female voice that responds or advises); and a clear sensation of a loving and gentle feminine presence. Some Mazatec believe this presence to be the Virgin Mary, while others believe her to be the goddess of plants and animals or the soul of Mother Nature itself. Other elements used during the ritual are beeswax candles, cocoa beans (considered a spiritual payment for the healing obtained), a mixture of lime and pulverized tobacco leaf called "San Pedro," and fresh flowers.

Both with sacred entities and with the rest of the beings, alive and dead, the Mazatec establish relations of reciprocity that allow them to unite the divine with the earthly things and to maintain the balance between the different forces and entities with which they share the territory. Well-being is asked of these entities in complex rituals where the *chjota chjine*, "the wise person who heals," or the *chjota chjine xkà*, "the wise person who cures with herbs," serves as a mediator between the worlds. For the Mazatec, disease is produced by an energy imbalance, a rupture in the established order, and a violation of the implicit agreement existing between humans and the settlers of the supernatural world, originated by negative feelings and thoughts or by entities that inhabit nature (Incháustegui, 1994). Women and men of knowledge feed the sick with fungi and plants, causing an altered state of consciousness that allows the individual, with the help of the healer, to become aware of and to detect the origin of their imbalance and to be restored using their will.

Nowadays, the Mazatec know that *S. divinorum* is smoked around the world, but some of them consider this to be wrong and against the spirit of the plant that should never be burnt. They believe that this practice is behind the misunderstandings regarding this herb and that it could be the cause of it being outlawed in some countries. When the Mazatec are asked about the addiction potential of the plant or about toxic or harmful effects, they clearly state that they and their ancestors have consumed *S. divinorum* for centuries, sometimes in amounts up to 100 pairs of leaves, without any problems, intoxications, or addictive behaviors. On the contrary, it is an invaluable source of healing for them. I also asked them about symptoms of paranoia or psychosis after its use, and I received the same answer: this never happened to them. But, for the Mazatec, the shamanic use of *xkà pastora* has to be taken seriously and approached carefully. One must have an honest intention of healing oneself or another or a plan to do good things with its use. A ritual with a beginning and end should be performed, and, even if the purpose is just to navigate

internal realms or to get to know the herb better, one must ask for permission of the spirit of the plant before cutting the leaves, be thankful, and show respect to its power.

Salvinorin A

S. divinorum owes its psychoactive properties to its active ingredient, the terpene salvinorin A (SA). SA was isolated and identified for the first time in 1982 in Mexico by Alfredo Ortega and his team, and shortly after by Valdés and his collaborators (Ortega, Blount, & Manchand, 1982; Valdes, Butler, Hatfield, Paul, & Koreeda, 1984). Daniel Siebert was the first researcher to investigate SA in humans (Siebert, 1994).

Pharmacological studies have shown that SA is a highly selective and potent kappa-opioid receptor (KOR) agonist (Roth et al., 2002). In fact, the exact structure of this receptor was described in detail thank to the highly precise binding of SA (Wu et al., 2012). The KOR and its endogenous ligands, the dynorphins, regulate the perception of pain in the human body; change in consciousness, mood, and control of the internal sensations of the body (interoception); and, in interaction with other systems, regulate the reward system of addictions (Chavkin, 2013, Schwarzer, 2009). SA is the only natural non-nitrogen compound currently known capable of acting as an agonist at the level of these opioid receptors. It is also one of the most potent psychoactive substances of natural origin known, being about 20 times more potent than psilocybin (the psychoactive component in numerous species of fungi), and in the range of potency of LSD. On the other hand, SA differs from other compounds capable of modifying perception, the so-called classic hallucinogens, such as mescaline, psilocybin, and LSD. The latter are alkaloids (nitrogenous compounds) and have affinity for the 5-HT_{1A} and 5-HT_{2A} receptors of serotonin. In my laboratory research administering SA to 32 volunteers, we have demonstrated, for the first time in humans, the involvement of opioidergic neurotransmission, rather than serotonergic, in the effects of SA in perception, cognition, and emotion (Maqueda et al., 2016).

About the subjective effects of the compound, in our laboratory studies, the inhalation of pure vaporized SA led to dose-dependent psychotropic effects of fast onset (less than 1 minute) and short duration (20 min). This is in contrast with the slow instauration and long duration of the effects following the Mazatec method of chewing the fresh leaves.

Perceptual modifications included the visual domain, and, in contrast with 5-HT_{2A} agonists, auditory hallucinations were very common. As one volunteer wrote in the trip report, “It was like a group of people shouting, especially female voices, and music was also playing.” A special type of visual-bodily synesthesia was also observed. While visual-auditory synesthesia is common with serotonergic and non-serotonergic substances, visual-proprioceptive synesthesia is rarely described (Luke & Terhune, 2013) and seems to be another unique feature of *S. divinorum*.

This effect was explained as seeing external modifications in reality like a wave that affects or folds the volunteer's body, or objects perceived with eyes open or closed were felt as being associated with the body: "A force was pressing the right side of my body . . . so my sensation was being a square. Visually I wasn't seeing any image, but that square was conceptually present in my mind." We observed lateralization of the effects, coming from a specific side of the body or reality: "I had the sensation that the effects of the substance were approaching me from the left." Also, in contrast with the classical serotonergic psychedelics, the loss of contact with external reality is prominent and dose-dependent. At the low (0.25 mg) and medium (0.50 mg) doses, there was an increase in bodily sensations, which means that the subjects experienced their body as safe and reliable, being able to pay more attention to the connection between emotions and physical states. A volunteer reported, "Warmth. I felt my body heavier, relaxed, with a subtle tingle on the neck and the head. My mind was also relaxed. I was connected with my body and with the sensations I was feeling. Very pleasant."

In contrast, high doses (1 mg) increased dissociation and loss of contact with the body and out-of-body experiences, like "I wasn't feeling that in that world I had a physical body. I was an energetic being." Our results suggest that KOR may play a previously underestimated role in the regulation of sensory perception, the interoception, and the sense of body ownership in humans. Other subjective effects reported included, in correlation with that of the Mazatec, physical sensations of being twisted, touched, or pushed and sensations of movement and of presences of beings or entities. Childhood memories were common and sensations of being in two realities at the same time: "I really wanted to be fully in that other reality, it was very familiar, like the reality of my childhood." The visions are not as organic as when the leaves are chewed; instead, volunteers refer to metallic objects, plastic surfaces, and mechanical artifacts. In our experiments, we also observed that SA increases the secretion of prolactin, antidiuretic hormone, and cortisol, and its subjective and physiological effects were blocked by the opioid antagonist naltrexone (Maqueda et al., 2015).

SA experience is clearly unique, with some correspondence with other psychedelics. As reported in an experiment led by Peter H. Addy, using dry leaves of *S. divinorum* potentiated with SA, the subjects compared the experience as similar to dreaming (43%); LSD (13%); psilocybin (10%); marijuana (10%); MDMA (10%); altered states of consciousness such as meditation, trance, or yoga (7%); or NMDA antagonists such as dextromethorphan (DXM) and ketamine (7%) (Addy, 2012).

In regard to safety of inhaled SA, laboratory studies show that doses of up to 12 mg of pure SA are safe in terms of physiological measures (Ranganathan et al., 2012). Of the 112 subjects in total, adding the participants of all the studies carried out in the world up to the present, from six laboratories of six different countries, adverse reactions were not found. On the contrary, volunteers reported liking the good effects and having positive and significant experiences. In general, the somatic side effects induced by SA, if they occur, are transient and do not cause excessive discomfort. These somatic-dysphoric effects are subjective changes in body

temperature and sensations of electricity and tingling in the body, which are similar to those of classic hallucinogens.

However, there is a lack of long-term studies. One of the reasons for this could be the low number of users that consume the plant repeatedly. Several surveys have revealed that nontraditional use of *S. divinorum* is sporadic and unremarkable due to unpleasant effects for the typical recreational consumption (Addy, Garcia-Romeu, Metzger, & Wade, 2015). There are two retrospective surveys of recurrent recreational users (Kelly, 2011; Nygård, 2007). Thirteen users (77% males) reported a greater connection with others, increased creativity, and connection with nature, as well as a greater understanding of the nature of reality (Nygård, 2007). However, these reports are limited because of their retrospective nature, relatively small sample size, and possible bias in recall. In one laboratory study with SA (MacLean, Johnson, Reissig, Prisinzano, & Griffiths, 2013), the researchers followed up 1 month after the experiment. Assessments showed no evidence of lasting negative effects, such as depression, anxiety, psychiatric symptoms, or visual impairment. In the open reports, no participant indicated lasting negative effects. Half of the participants reported specific positive changes which they attributed to the experience with SA, including increased self-confidence, a feeling of greater physical comfort and calm, less emotional reactivity, improved interpersonal relationships, and a renewed interest in daily responsibilities. Bücheler and colleagues (Bücheler, Gleiter, Schwoerer & Gaertner, 2005) reported the case of a 19-year-old man in Germany who was a user of *S. divinorum*. The young man smoked or chewed the leaves twice a week for 6 months, without detrimental effects on his health and social or academic life. He described having experienced effects of floating, feelings of having solved personal or philosophical problems, itching, and ringing in the ears. He did not report any negative psychological effects and described a gradual tolerance over the 6-month period.

We have also investigated the neurophysiological correlates of SA effects in humans, measuring spontaneous brain oscillations (EEG) before and after the administration of 1 mg of vaporized SA. The results showed a unique pattern of neurophysiological effects. SA suppressed the alpha rhythm and markedly increased slow delta activity. Less prominent effects included increases in the theta and low gamma bands. While SA shares with serotonergic psychedelics the alpha-suppressing action, its main neurophysiological signature is an atypical enhancement of slow delta activity.

About the neural substrates of SA, in the brain are high levels of KOR in the neocortex, in the thalamus, and in the ventral tegmental area. The agonism of the KOR in the temporal and parietal cortex could be the cause of the visual and auditory modifications (temporal cortex) and of the altered experience of the body (parietal cortex). In addition, the medial posterior parietal cortex is a key structure within the default mode network (DMN), which has been proposed as associated with the inner sense of self (Raichle, 2011; Raichle et al., 2001) or with the embodied self. The claustrum, a layer of neurons near the insula, also shows high levels of KOR. From studies with SA, researchers have proposed that SA could interrupt the processes of brain integration that take place at this level and lead to the effects of disconnection

with reality, naming the claustrum as "the gate of consciousness" (Stiefel, Merrifield, & Holcombe, 2014).

In the leaves of *S. divinorum* are other terpenes, such as divinatorins, salvinorins, salvinicins, and salvidivins, whose role in the pharmacological effects is not yet elucidated. They also contain loliolide (a potent ant repellent); hardwickiic acid and (E)-phytol, both with antimicrobial and antibacterial (*Staphylococcus aureus* and *Candida albicans*) properties; and nepetoidin B, with antifungal properties (Casselman, Nock, Wohlmuth, Weatherby, & Heinrich, 2014).

Therapeutic Potential

KOR agonists such as SA have applications for multiple ailments, and SA is extremely affine, potent, and precise when it comes to binding to these brain receptors. Some of the valuable medications that could be developed from *S. divinorum* are:

- Safe analgesics without addictive properties: The efficacy of SA as an analgesic has been demonstrated in animal studies (Guida et al., 2012). In current medical practice, sometimes very powerful analgesics like morphine are used, which are habit forming and produce dependence. This is not the case with SA. In fact, research has shown that SA has anti-addictive properties (Serra et al., 2015).
- Anti-inflammatories: It has been demonstrated in animal studies that SA has ultra-potent effects on macrophages via the KOR and CB1 receptors and exerts an important attenuation of inflammation and antipruritic effects. SA inhibits intestinal motility and reduces abdominal pain in the irritable bowel syndrome. In recent studies with mice, SA has been shown to inhibit the leukotriene-mediated inflammatory response. Leukotrienes are crucial in various autoimmune and inflammatory conditions such as urticaria, bronchial asthma, allergic rhinitis, and cardiovascular problems (Aviello et al., 2011; Rossi et al., 2016).
- Medications to treat different types of cancer: When there are tumors in the brain, one of the difficulties of therapeutics is to get the drugs through the blood-brain barrier and reach the tumor. The terpene SA is able to cross the blood-brain barrier and reach the brain and structures of the CNS in less than a minute. SA analogs have demonstrated antiproliferative properties, inhibiting the growth of 77–86% of tumor cells in breast cancer (Vasiljevik, Groer, Lehner, Navarro, & Prisinzano, 2014).
- Medications for disorders such as schizophrenia, bipolar disorder, and Alzheimer's disease: It is clear that the KOR-dynorphin system plays a key role in modulating perception and human consciousness. This suggests the possibility that new compounds derived from SA could be effective for the treatment of these disorders that are manifested by alterations of perception (Butelman & Kreek, 2015; Tejeda, Shippenberg, & Henriksson, 2012).

- Antidepressants: Animal studies have shown antidepressant properties of SA, and it has been proposed as an ideal candidate for the treatment of major depressive disorder (Taylor & Manzella, 2016). Regarding human subjects, K. R. Hanes (Hanes, 2001, 2003), in Australia, presented a case report of a 26-year-old woman with a long treatment-resistant depression who showed improvement after taking sub-psychoactive oral doses of *S. divinorum* leaves. The patient chewed and held in the mouth 0.5 to 0.75 grams of dry leaf for 15–30 min, two or three times per week. The patient also claimed to benefit from occasional psychoactive doses of *S. divinorum* consisting of 2–4 g of leaves taken following the same method as the previous one. Dr. Hanes reported on the patient's total remission of depressive symptoms in the past 6 months, in addition to a considerable improvement in self-esteem and psychospiritual development. Later, Hanes wrote a follow-up report in which he described six additional patients who reported obtaining complete remission of symptoms in treatment-resistant depression using the leaves of *S. divinorum*. Sadly, Australia was the first country to outlaw *S. divinorum* in 2002.
- Medication to treat psychostimulant abuse: Animal research has revealed that SA reduces dopamine levels in parts of the basal ganglia, disrupting many of the effects of cocaine and the addiction cycle. In the experiments with rats, SA does not seem to suppress their movement, the action of pushing the lever to drink, or their motivation before stimuli. In contrast, SA appears to specifically suppress cocaine-related behaviors and motivations (Dos Santos, Crippa, Machado-de-Sousa, & Hallak, 2015). Western medicine has developed—with questionable success—pharmacological treatments for the abuse of opiates, alcohol, and tobacco, but there is currently no treatment for the abuse of psychostimulants, so research with SA hold the promise to help millions of addicts. However, it is very important to remember that the traditional use of *S. divinorum* by the Mazatec to successfully treat a complex and multifaceted problem like addiction is part of a ritual and a much larger, organic, and inclusive worldview than our compartmentalized interventions and that the properties of this herb cannot be reduced to the pharmacological mechanism of just one isolated component in the form of a pill.
- Assisting psychotherapy: *S. divinorum* has several properties that would make it effective as an adjunct to psychotherapy. As we have seen, in low and medium doses, it helps to increase awareness of the body and of the interconnectedness of emotions and mental states. It also produces a state of deep introspection, facilitates the recall of biographical episodes, and offers access to areas of the psyche that are not easily attainable ordinarily. This possible psychotherapeutic use is not new; even if shamanism and psychotherapy are not the same thing, during the ceremonies with this particular plant, the Mazatec establish a dialogue between patient and healer, posing questions during the ceremony until the problem and the possible solution are elucidated. Also, low doses have been used for enhancing meditation work, finding unusual clarity of mind, and enhancing the ability to concentrate (Soutar & Strassman, 2000). From the trip reports

from volunteers in one of our studies, "The state of peace obtained allowed me to think in a very lucid way" (Maqueda et al., 2015).

Other promising medications are neuroprotectors for a number of acute brain pathologies accompanied by a vasoconstrictive event (Su, Riley, Kiessling, Armstead, & Liu, 2011) and short-term anesthetics that do not depress breathing, safer than the anesthetics that are used today (McCurdy, Sufka, Smith, Warnick, & Nieto, 2006).

How to Use *Salvia divinorum*

Learning from the Mazatec, in the best possible scenario, somebody interested in using *S. divinorum* for medicinal, psychotherapeutic, or inner exploration purposes should grow their own cuttings at home. This would create a direct relationship with them, as we both are living beings in mutualistic existence, like humans and plants have always coexisted. Cuttings can be bought online, and they are relatively easy to grow. Nursing and touching them, witnessing them growing (and maybe flowering), and honoring this teacher plant that is giving us so much would be the fundamental relationship that we could create at home to approximate the loving appreciation of the Mazatec toward *S. divinorum*. To perform a ritual before harvesting and consuming the leaves, with simple constitutive elements and personal thoughts, would simulate the Mazatec "set and setting" by an act that opens and closes the ingestion of a mind-altering herb that gives access to the unknown.

To chew its crunchy and velvety fresh leaves is an ideal method of consumption to begin with; it provides a very rich and totally unique experience and is easily manageable. Sounds and lights can interrupt the trip, and the effects start very subtly. Therefore, it is very important to remain in a meditative state and in complete darkness and to wait for the effects. The sounds heard in the Sierra are of a forest at night, running water, and usually rain. There is some inverse tolerance, so if the effects are not attained in the first tries, they could be achieved in consecutive attempts. The Mazatec microdose with small leaves when feeling low energy levels or to enhance mood, and the microdosing approach could be a good way to prepare the body for a ceremony with more leaves. The quantity of SA per leaf can vary depending on the size of the leaves and on the potency of the strain, and since individual sensitivity is highly variable too, due to genetic and gender differences with the KOR (Schmidt et al., 2005), it is better to start with small amounts until the personal sensitivity to the substance is known. Peltate glandular trichomes, which contain SA, are present only on the abaxial surface of the leaves (Siebert, 2004).

As bigger amounts of leaves are required to attain stronger effects or to follow a weekly treatment, dry leaves can also be bought online. In my own practice with the Mazatec, I have had noticeable psychedelic effects with 6–8 leaves of medium size. My chewing method could be applied for dry leaves too: to break the leaves in little pieces with the incisors and moisten them well with saliva while moving them with

the tongue all around the inside of the mouth. The leaves could be eaten in pairs of two like a sandwich bent in the middle, accumulating the well-chewed wet plant material in the upper gums and eating the next two leaves and so on. The excess of saliva that will be produced could be used to moisten again the plant material accumulated in the gums instead of being swallowed. More leaves can be eaten as desired for bigger effects or to prolong the effect, but keep in mind that the effects will appear in about 20–30 min or more. Before chewing the leaves, it could be useful to brush the mouth to remove dead cells and to use a mouthwash with alcohol, to increase the permeability of the mucous membranes. External applications of poultices can be previously moistened in water or applied with alcohol as the Mazatec do.

Strong and high-quality tinctures can be bought online or can be made at home following extraction methods of variable difficulty. They are a good way of experiencing the effects like the traditional Mazatecs, with effects starting slowly and remaining longer. To attain psychedelic effects, the leaves or tinctures must be in contact with the oral mucosa, because enzymes in the intestinal tract rapidly degrade SA. Interestingly, pure SA alone is not sublingually active, but it is when the leaves are chewed. Could some of the other terpenes present in the leaf work as a catalyst? More research is needed to unveil *S. divinorum*'s mysteries and to investigate further the greater bioavailability of SA in other solvents. Future work might test other dosage forms, like patches targeting the oral mucosa for rapid delivery of high doses when it's therapeutically needed, which may allow maintenance of therapeutic drug levels in the brain (Orton & Liu, 2014).

In regard to the most potent and fastest method of attaining psychedelic effects, that is, smoking SA-enhanced leaves, or potentiated extracts, we should know by now that *S. divinorum* and SA can be dangerous if used irresponsibly, like any other substance that alters consciousness. It is one of the most potent psychedelics, and smoking high doses can make one forget that one has a body while navigating internal landscapes. From our neurophysiological results, we know that 1 mg of pure SA puts the brain for a few minutes in a deep sleep state, but the body is still able to move. So it is imperative to be accompanied by a sober and attentive sitter. While smoking plain dry leaf, it can be difficult to achieve strong effects because of the large quantities of smoke that must be inhaled. This is easier to achieve with the SA-enhanced leaves. For managing the potentiated extracts, it is very important to have a precision scale to measure milligrams and to start with the lowest strength. Starting with low doses and slowly dosing up is a really good way to become familiar with the effects. Patience, information, and the precision scale are all what is needed to have an enjoyable and unique experience smoking this extraordinary herb while visiting what is called by psychonauts around the globe "the *Salvia* space." This plant is high technology for the mind, an invaluable tool to put to test the fabric of reality and to explore the wonders of human consciousness. As D. M. Turner put it in his book, *Salvinorin: The Psychedelic Essence of Salvia divinorum* (1996, para. 1), "If there is a physical counterpart to consciousness, memory or identity in humans, and if it could be extracted from our brains, I think we would find something similar to salvinorin."

I strongly recommend visiting the *Salvia divinorum* Research and Information Center, managed by the expert Daniel Siebert, to learn how to calculate dosing and other important details to take into account when smoking.[1] Some extraordinary reports written by a highly experienced psychonaut smoking very high doses of potentiated extracts that may be of interest can be found in the blog, A World Out of Mind.[2] Trip reports of experiences with fresh leaves and other methods and ideas of consumption can be found in the special journal of *The Entheogen Review* dedicated to *S. divinorum* and SA (Aardvark, 2002). I have created the nonprofit "Xkà Pastora," dedicated to the ethnobotanical conservation of *S. divinorum*, where my fieldwork can be followed.[3] The Mazatec Sierra, the natural sanctuary of *Salvia*, still has secrets to unveil. How many different varieties could have wildly emerged from seeds during the centuries, and with what properties? Current research is studying only one of them! What are the long-term effects of *Salvia* among the Mazatec? Is there a Mazatec elder that still remembers the native name of the herb? Are there any particular chants sung during ceremonies with the plant? Ideas that are worth consideration for future explorers.

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[1]The *Salvia divinorum* Research and Information Center, sagewisdom.org

[2]A World Out of Mind, salviaspace.blogspot.com

[3]Center for Research and Ethnobotanical Conservation of *Salvia divinorum*, xkapastora.org

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