

## Toxicology Rounds



# Salvia divinorum: A Unique Hallucinogen



By Leon Gussow, MD

When Brett Chidester, a 17-year-old high school senior living in Delaware, committed suicide earlier this year, his parents attributed the tragedy in part to his use of *Salvia divinorum*, a little-known but potent hallucinogen that is still legal in most states. Their belief, although speculative, did gain some support from an essay Brett had written about his experience with the drug. “*Salvia* allows us to give up our senses and wander in the interdimensional time and space,” he wrote. “Also, and this is probably hard for most of us to accept, our existence in general is pointless. Final point: Us earthly humans are nothing.”

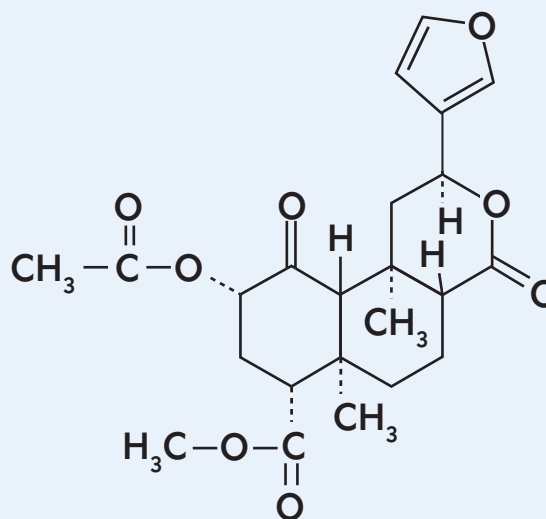
*S. divinorum*, a perennial herb native to northeastern regions of the state of Oaxaca in Mexico, has been used for centuries by the Mazatec Indians in divination and healing rituals. It contains salvinorin A, which has been called by some — erroneously — the most potent of all naturally-occurring hallucinogens. Unlike other mind-altering substances, salvinorin A is not an alkaloid, does not contain nitrogen, and does not interact with the serotonin (5-HT<sub>2A</sub>) receptor. Rather, it is a high-affinity and selective agonist of

the kappa opioid receptor. No other known hallucinogen has a similar structure or mechanism of action.

Research with other kappa agonists has demonstrated that they have some analgesic properties, but unlike mu-opioid agonists such as morphine and heroin, they do not produce respiratory depression or addiction. They also can cause psychotic-like behavior and dysphoria. Pfeiffer et al (*Science* 1986;233:774) administered an intravenous benzomorphan kappa agonist to 30 male volunteers. Low doses produced somatic complaints such as weakness, diaphoresis, dizziness, and anxiety, along with feelings of body distortion and discomfort.

Higher doses caused disturbances in the perception of time and space, visual distortions, feelings of depersonalization, and loss of self-control. Some subjects became disoriented and seemed unaware that they were taking part in an experiment. The authors report that these psychotomimetic effects were most apparent

### CHEMICAL STRUCTURE OF SALVINORIN A



Source: Adapted from *Forensic Sci Int* 2000;112:143.

during the first 30 minutes after drug injection, and were prevented by pretreatment with naloxone.

*S. divinorum* is not effective if ingested because salvinorin A is deactivated in the gastrointestinal tract. Traditionally the leaves are chewed and held in the mouth, allowing the hallucinogen to be absorbed

slowly through the oral mucosa. By this route, effects occur within five or 10 minutes, plateau for about an hour, and then gradually decrease over the next hour. When the leaves are smoked, effects occur much more rapidly, generally peaking within several minutes and lasting about half an hour. Higher doses, such as those achieved by salvinorin A extract, cause more prolonged symptoms. Because this is a largely unregulated drug, both the leaves and the extract are available for sale on the Internet. As of May, *S. divinorum* and salvinorin A were classified as controlled substances only in Delaware, Louisiana, and Missouri. On a national level, the U.S.

Drug Enforcement Administration considers them “drugs of concern,” but does not limit their distribution. *S. divinorum* is banned in Australia, Denmark, and Italy.

Anecdotal descriptions by those using the drug have reported visions of people, objects, and places as well as out-of-body experiences and the illusion of traveling back in time. Siebert (*J Ethnopharmacology* 1994;43:53) listed some common themes to these visions and sensations:

- Becoming objects (yellow plaid French fries, fresh paint, a drawer, a pant leg, a Ferris wheel, etc.).
- Visions of various two-dimensional surfaces, films, and membranes.
- Revisiting places from the past, especially childhood.
- Loss of the body or identity.
- Various sensations of motion or of being pulled or twisted by forces of some kind.
- Uncontrollable hysterical laughter.
- Overlapping realities. The perception that one is in several locations at once.

Because the sensations caused by salvinorin A are frequently unpleasant, some users try it once, consider it a “bad trip,” and do not wish to revisit the experience. Recurrent users tend to take the drug in a solitary and quiet setting. Crowds of people and loud music typically increase the dysphoric effects of *S. divinorum*, so it is not commonly used as a party drug.

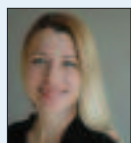
Although intense, the mind-altering effects of salvinorin A are relatively brief, making it unlikely that physicians will encounter acutely intoxicated patients in the emergency department. There have been no published clinical reports concerning *S. divinorum* exposure. Laboratory studies on human volunteers suggest that naloxone reverses many of the effects caused by salvinorin A. Because the drug has such a short duration of

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## Quick Consult



### Symptoms: ‘Anxiety Attack’ with Profuse Sweating and Resting Tremors



By Jennifer L. Wiler, MD, MBA

A 54-year-old man presents to the ED with his brother, who is concerned that the man is “having an anxiety attack.” The patient is a paranoid schizophrenic who takes clonazepam (Klonopin), quetiapine (Seroquel), and sertraline (Zoloft). He ran out of clonazepam three days before, and has now developed profuse sweating and resting tremors.

He felt “anxious,” and took approximately 15 escitalopram (Lexapro) tablets from an expired prescription “to relax.” He denies any suicidal ideations. He brought the bottle of escitalopram to the ED, which shows that the prescription expired a year before. The brother reports that the patient is at his baseline mental status.

The patient denies chest pain, palpitations, fevers, headache and eye complaints, rash, abdominal pain, diarrhea, weakness, and the use of street drugs. He is afebrile, normotensive, tachypnic at a rate of 27, and in normal

sinus rhythm. On exam, he is markedly diaphoretic (see photograph) with 5 mm dilated reactive pupils and no nystagmus. His neurological exam is significant for a resting tremor (most prominent in his hands), ataxia, and lower extremity rigidity with clonus at the ankles (see photograph).

What is this patient’s diagnosis, and what is causing his symptoms? See p. 26.



## Legal Notes



# Will EPs' Reluctance to Embrace Thrombolysis for Stroke Lead to Lawsuits?



By Jonathan Glauser, MD, MBA

A 66-year-old man presents with weakness and dizziness. The triage note says that he is a poor historian. There is no bed available immediately, and 35 minutes later his daughter arrives and says that he has speech difficulty he did not have three hours before. He is placed in a room, where some left-sided weakness is noted, which probably can be dated in onset to two hours prior to arrival in the emergency department.

You obtain a head CT, which shows no acute bleed or effacement of sulci. The ED has access to teleradiography, and the radiologist sees no gross abnormality. It now has been three hours and 40 minutes since stroke onset, and the patient is admitted to a staff neurologist, the third one you called. The patient ultimately regains the ability to walk normally, but he still has some difficulty with speech and swallowing, and does not regain full use of his left side.

He is retired, but claims that he cannot play the piano or sing in the men's choir. The family asks about a miracle stroke drug that can be given in the ED to reverse all neurologic deficits, but by the time you receive an official CT report, the three-hour time window has elapsed. You are somewhat relieved because you do not work at a stroke center, you have doubts about the quality of the neuroradiologic skills of your radiologists, and you know that your staff neurologists are, to say the least, not aggressive. A lawsuit is filed by the family.

### Ischemic Stroke

Ischemic stroke is a major medical problem in the United States, where approximately 600,000 new cases occur each year. In the United States and Canada, stroke is the third leading cause of death, with an age and sex adjusted incidence

of approximately 1000 per 100,000 in the 65- to 74-year-old group and approximately 2000 per 100,000 in the 75- to 84-year-old group. (*Stroke* 1999;30:2523.) If blood flow to a specific region is restored within a critical time frame, there is func-

tional recovery of the ischemic penumbra. The hypothesis that intravenous thrombolytic therapy may restore blood flow and improve outcome in acute ischemic stroke was not tested in large randomized trials until the 1990s.


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### Part 1 in a Series

## SALVINORIN A

*Continued from previous page*

action, talking the patient down in a quiet setting with calm reassurance would most likely result in rapid resolution.

After the publicity surrounding the suicide of Brett Chidester and its possible connection to his use of *S. divinorum*, there has been increased interest in banning sale and distribution of the drug. This will almost certainly become much more tightly controlled in the future. Already, laws banning *S. divinorum* have been proposed in New York, New Jersey, Illinois, Tennessee, Oklahoma, and Alaska. It would be surprising if the DEA did not take action in the near future. 

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