The ENTHEOGENS & DRUG POLICY PROJECT

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A Prominent *Salvia Divinorum* Researcher Speaks Out: Letter to Congress

RE: Bill H.R. 5607

Dear Honorable Member of Congress:

This letter summarizes the important medicinal properties of *Salvia divinorum* and its primary active constituent salvinorin A. It also puts forth several objections to bill H.R. 5607, which inappropriately seeks to place this medicinal herb in Schedule I of the Controlled Substances Act.

As a pharmacognosist who has devoted the last ten years to the scientific study of this herb, I believe that I am particularly qualified to speak on this issue. I was the first person to investigate the human pharmacology of salvinorin A and to clearly identify this compound as the psychoactive principle of *Salvia divinorum* (Siebert, 1994). Most recently, I coauthored a paper published in *Proceedings of the National Academy of Sciences (PNAS),* in which my research group reported our findings regarding the neurological mechanism of salvinorin A's action. These findings are of particular significance because they provide solid evidence for the medicinal value of this compound. I am currently working in collaboration with several other scientists on various avenues of scientific investigation into the pharmacology of salvinorin A and closely related compounds. My collaborators include Dr. Bryan Roth (Project Director of the National Institute for Mental Health Psychoactive Drug Screening Program) and Dr. Michael J. Iadarola (Chief of the Neuronal Gene Expression Unit at the Pain and Neurosensory Mechanisms Branch of the National Institute for Health). In addition to my scientific endeavors, I am presently completing work on a comprehensive book about *Salvia divinorum*.

Medical properties

There are approximately one thousand species of *Salvia* worldwide. *Salvia divinorum* is just one of the many species that are recognized for their useful medicinal properties. The common name for all salvias is *sage.* Most people are familiar with the common culinary sage, *Salvia officinalis,* which in addition to its usefulness as a flavoring agent, is also used for its medicinal properties. The genus name *Salvia* is derived from the Latin *salvare*, meaning "to heal" or "to save." The words *salvation* and *savior* also come from this same root.

Salvia divinorum is endemic to the Mazatec Sierra of central Mexico, where it has a long history of medicinal use. It is used both for its psychoactive properties and as an effective treatment for arthritis, headache, and eliminatory complaints. The validity of each of these different applications is well supported by my research group's recent pharmacological findings.

To summarize our recent findings: Salvinorin A is a uniquely potent and highly selective kappa-opioid receptor agonist, and as such, it has tremendous potential for the development of a wide variety of valuable medications. The most promising of these include safe non-addictive analgesics, antidepressants, short-acting anesthetics that do not depress respiration, and drugs to treat disorders characterized by alterations

in perception, including schizophrenia, Alzheimer's disease, and bipolar disorder (Roth *et al.,* 2002).

Kappa-opioid receptor agonists are of particular interest to pharmacologists because they provide effective pain medications that are not habit forming and do not produce dependence. In fact, there is a growing body of evidence that indicates that kappa-opioid receptor agonists are actually "aversive"—the opposite of addictive. This is an important advantage over most powerful analgesics currently prescribed. My colleagues and I will soon be publishing a paper that reports the results of animal studies that demonstrate the effectiveness of salvinorin A as an analgesic (Chavkin *et al.,* in press). In my book I describe many case reports in which people testify to the effectiveness of this herb for managing pain. The traditional Mazatec use of *Salvia divinorum* to treat headaches and arthritis also attests to its efficacy as an analgesic.

The ability of salvinorin A to block perception of pain also suggests that it may prove quite useful as a short-acting general anesthetic. The fact that it does not depress respiration is particularly interesting, because it indicates that salvinorin A could be much safer than most general anesthetics currently in use.

Recently Dr. Karl Hanes published a case report in the *Journal of Clinical Psychopharmacology, i*n which he describes a patient that obtained relief from chronic depression by using *Salvia divinorum* (Hanes, 2001). In my book I describe several additional accounts of people who have recovered from serious depression with the help of this herb. It is especially interesting that these people were able to obtain persistent relief from their depression after only a few treatments. Quite unlike the continuous medication regime required with conventional antidepressants such as Prozac—which in most cases only offer symptomatic relief from depression—*Salvia divinorum* often produces long-lasting clinical improvement.

Because salvinorin A alters various perceptual modalities by acting on kappa-opioid receptors, it is clear that these receptors play a prominent role in the modulation of human perception. This suggests the possibility that novel psychotherapeutic compounds derived from salvinorin A could be useful for treating diseases manifested by perceptual distortions (e.g. schizophrenia, dementia, and bipolar disorders). This is a promising area of research that is important to pursue further.

Salvia divinorum has several properties that make it useful in psychotherapy: it produces a state of profound self-reflection, it improves one's ability to retrieve childhood memories, and it provides access to areas of the psyche that are ordinarily difficult to reach. I have spoken with several psychotherapists who have used this herb in their practice. They are impressed with its effectiveness as a psychotherapeutic tool. This type of application is not new—the Mazatecs have long used *Salvia divinorum* to treat psychological complaints.

Salvinorin A is also an important neurochemical probe for studying the dynorphin/kappa-opioid-receptor system. As such, it is useful for research into the neurological mechanisms of perception and awareness. Salvinorin A is remarkable in that it belongs to an entirely different chemical class than any previously identified opioid receptor ligand (it is a diterpenoid). This fact is of great interest to pharmacologists because it opens up a vast new area for future drug development.

No significant abuse potential

There are many popular misconceptions about *Salvia divinorum*. Presumably, bill H.R. 5607 is based on some these. Many of these misconceptions have their origin in a few sensationalistic articles that have appeared in the popular press, and others derive from the absurd advertising claims of unethical herb vendors who deliberately exaggerate the effects of *Salvia divinorum* in an effort to increase sales.

The fact is that the effects of *Salvia divinorum* are not appealing to recreational drug users. The majority of people who try it find that they do not enjoy its effects and do not continue using it. People who use it medicinally take it infrequently. It is not euphoric or stimulating. It is not a social drug. Since it increases self-awareness, it is useless as an escapist drug. It is most useful as a medicinal herb.

Salvia divinorum is not addictive or habit forming. Its mechanism of action indicates that it may actually be anti-addictive. Many people have reported that *Salvia divinorum* actually helped them to overcome substance abuse problems.

Safety

Salvia divinorum is non-toxic. Toxicological studies have been performed by Dr. Leander Valdés at the University of Michigan, Jeremy Stewart at the University of Mississippi, Dr. Frank Jaksch of Chromadex Inc., and Wayne Briner of the University of Kansas. Neither *Salvia divinorum* nor salvinorin A showed toxicity in any of these studies. There is a vast body of empirical evidence that indicates *Salvia divinorum* is a remarkably safe herb. Indeed, the Mazatecs, who have probably used *S. divinorum* for hundreds of years, do not attribute any toxic properties to this plant.

Conclusions

Salvia divinorum is a relatively obscure medicinal herb with no significant abuse potential. It does not present a risk to public health or safety. Criminalizing it would only serve to create a problem where one did not previously exist. The regulation of herbal medicines such as this is a matter that should be handled by the FDA, not the Controlled Substances Act.

There is no reasonable justification for making *Salvia divinorum* a controlled substance. Placing it in schedule I would deprive people of a safe and useful medicinal herb, and it would seriously hamper promising medical research. Because of its complex stereochemistry, salvinorin A is virtually impossible to produce synthetically. It is important that its source plant, *Salvia divinorum,* remain available so that researchers can continue to study this important compound.

Evidently, this bill is based on inaccurate information about *Salvia divinorum*. Schedule I is intended for substances that have a high potential for abuse, a lack of accepted safety, and no currently accepted medical use. *Salvia divinorum* does not meet any of these criteria.

Sincerely,

Daniel J. Siebert

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