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Salvia divinorum: an hallucinogenic mint which might become a new recreational drug in Switzerland

C. Giroud[a,*], F. Felber[b,d], M. Augsburger[a,c], B. Horisberger[a], L. Rivier[a], P. Mangin[a]

[a]*Laboratoire de Toxicologie Analytique, Institut Universitaire de Médecine Légale, rue du Bugnon 21, 1005 Lausanne, Switzerland*
[b]*Institut de Botanique de l'Université, Neuchâtel, Switzerland*
[c]*Center for Human Toxicology, University of Utah, Salt Lake City, UT, USA*
[d]*Jardin Botanique de l'Université et de la Ville, Neuchâtel, Switzerland*

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Abstract

Salvia divinorum Epling & Jativa is an hallucinogenic mint traditionally used for curing and divination by the Mazatec Indians of Oaxaca, Mexico. Young people from Mexican cities were reported to smoke dried leaves of *S. divinorum* as a marijuana substitute. Recently, two *S. divinorum* specimens were seized in a large-scale illicit in-door and out-door hemp plantation. Salvinorin A also called divinorin A, a *trans*-neoclerodane diterpene, was identified in several organic solvent extracts by gas chromatography–mass spectrometry. The botanical identity of the plant was confirmed by comparing it to an authentic herbarium specimen. More plants were then discovered in Swiss horticulturists greenhouses. All these data taken together suggest that many attempts exist in Switzerland to use *S. divinorum* as a recreational drug. This phenomenon may be enhanced because neither the magic mint, nor its active compound are banned substances listed in the Swiss narcotic law.

Keywords: Hallucinogenic plants; *Salvia divinorum*; Salvinorin A; GC–MS

1. Introduction

During a recent fire of a private home, two unknown coleus-like shrubs at the

*Corresponding author. Tel.: +41-21-314-7086; fax: +41-21-314-7090.
E-mail address: christian.giroud@inst.hospvd.ch (C. Giroud).

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vegetative stage were found together with an illicit, indoor, large-scale hemp cultivation. A plant sample was collected and subjected to botanical and chemical investigations.

2. Botany

The unknown plants were about 0.5 m in height. The leaves were about 15 cm long, ovate, dentate and acuminate, opposite and decussated. The fleshy stems were quadrangular with characteristic flanged angles. Their morphology was typical of plants belonging to the Lamiaceae family.

3. Toxicological analyses

All chemicals and solvents used were analytical reagent grade.

3.1. Equipment and chromatographic conditions

For screening investigations, a Hewlett-Packard (HP) Series 5890 series II plus gas chromatograph was used in combination with a HP MSD Series 5971 mass spectrometer, a HP 7673 Series injector and a HP Vectra XM Series 4 workstation (GC–MS). The GC conditions were as follows: splitless injection mode (purge time: 1 min); HP Ultra-2, 5% phenyl-methyl-silicone capillary column (25 m $\times$ 0.2 mm I.D., 0.33 μm film thickness); column temperature, programmed from 70°C (initial time: 3 min) to 190°C (rate: 20°C/min) and then to 305°C (rate: 10°C/min, final time: 11.0 min); carrier gas: helium, constant flow-rate: 1.2 ml/min; injection port temperature: 260°C.

The MS conditions were the following: scan mode (40–400 a.m.u., threshold: 50, 1.3 scan/s from 3 to 7 min and 40 to 550 a.m.u., threshold 50, 0.9 scans/s from 7 to 31.5 min); ionization energy, 70 eV; MS interface and MS temperatures 280 and 180°C, respectively; EM offset: 200 V above the tune value. Data were automatically processed with macro-programs which comprise peak search and tentative identification with the Pfleger, Aafsdrug, Nbs75k, Wiley138 and our own spectra libraries.

3.2. Extractions

3.2.1. Fresh material

About 100 mg of fresh leaves were ground with a mortar and a pestle in the presence of 2 ml saturated ammonia buffer (pH 9.5). After addition of 2 ml of chloroform/isopropanol (9:1, v/v), the mixture was shaken for 30 min. Phase separation was achieved by centrifugation. The organic phase was collected and evaporated under N_2 at 40°C. The dried residue was acetylated with 100 μl acetic anhydride/pyridine (3:2, v/v) for 30 min at 60°C. The solvent was taken to dryness and the plant extract dissolved into 100 μl ethyl acetate. One μl was subjected to gas chromatography–mass spectrometry analysis (GC–MS).

3.2.2. Dried material

The plant material was air-dried under pressure for several days. Then, 100 mg of dried leaves were crushed, mixed with 3 ml methanol and sonicated for 0.5 min. The powder was then extracted for 30 min on a horizontal shaker. After paper-filtration (Schleicher & Schuell 595 round filters) on a Buchner funnel, rinsing with 2 ml of fresh methanol, the extract was taken to dryness with N_2 at 40°C and dissolved in 100 μl acetonitrile. One μl was subjected to GC–MS.

4. Results

Beside sugars, fatty acids, vitamins and plant sterols, one mass spectrum from the total ion chromatogram of the acetylated basic extract of the fresh plant was tentatively identified as divinorin with the Wiley database. This compound turned out to be a furanolactone neoclerodane diterpene already known as the main active drug of *Salvia divinorum*, a plant belonging to the Lamiaceae family. Its chemical structure is shown in Fig. 1. Divinorin [1] is also called divinorin A, its chemical structure is identical to salvinorin A, a molecule which was previously described by Ortega et al. [2]. Divinorin B or salvinorin B refer to their desacetyl analog [1].

Neophytadiene, alcanes, tocopherol, stigmasterol, fatty acids and salvinorin A were detected in the methanolic extract of the dried plant. The total ion chromatogram and the mass spectrum of salvinorin A are shown in Figs. 2 and 3, respectively. Salvinorin A occurred as a major peak at the end of the chromatogram (retention time: 23.5 min). The base peak of its mass spectrum was $m/z=94$ and the putative molecular ion $m/z=432$ corresponding to the raw structure $C_{23}O_8H_{28}$. Other significant ions were $m/z=55$, 107, 121, 166, 220, 273, 318, 359 and 404. This mass spectrum is similar to those reported for salvinorin A isolated from the pharmacologically active fractions of purified *S. divinorum* extracts or by chromatography of a hot chloroform extract [1,2].

Salvinorin A was also detected by GC–MS in the methanolic extract of a plant cultivated by a horticulturist as *S. divinorum* (results not shown).

The detection of salvinorin A (which is acetylated on its diterpenic nucleus) in both the acetylated basic extract and the methanolic extract indicate that the seized plant

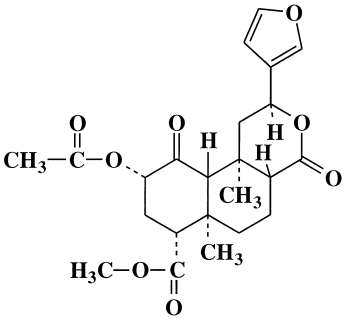

Fig. 1. Chemical structure of salvinorin A (=divinorin A).

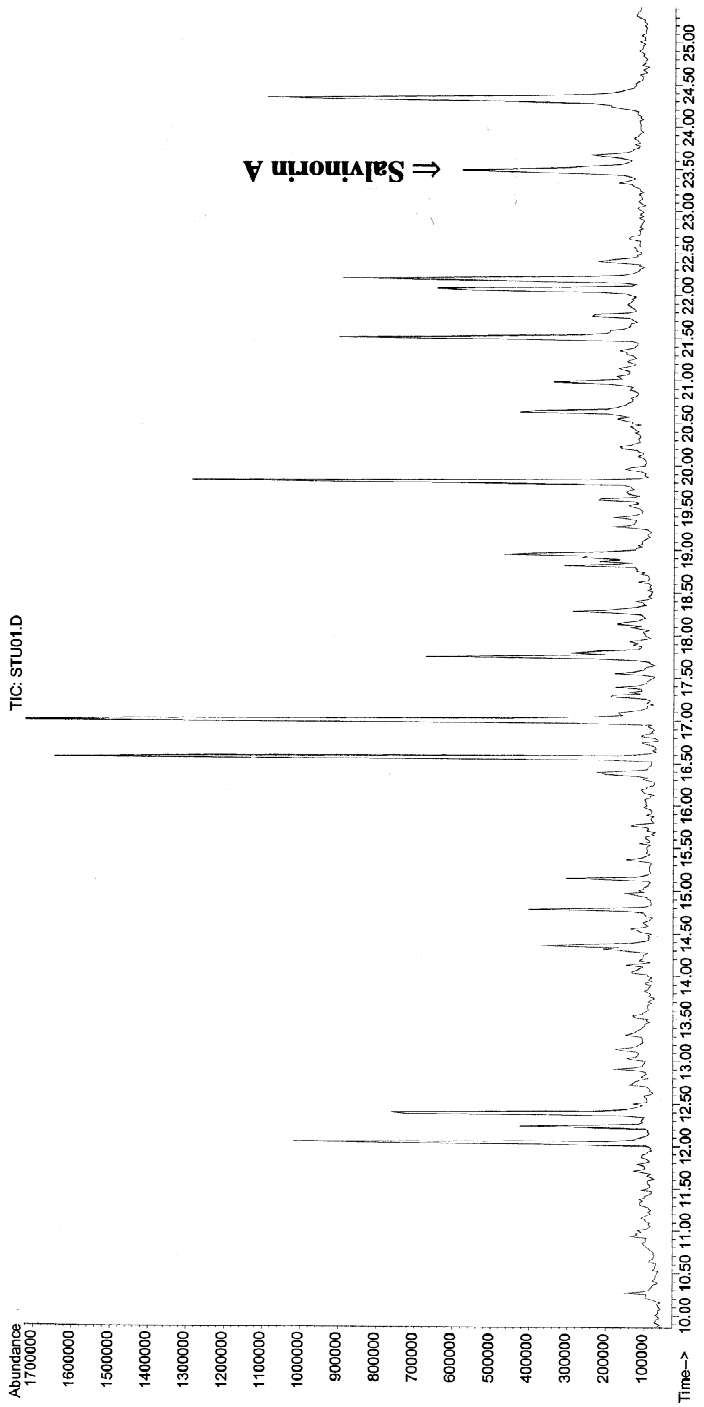

Fig. 2. Total ion chromatogram of a methanolic extract of a Lamiaceae identified as *Salvia divinorum* Epling & Jativa.

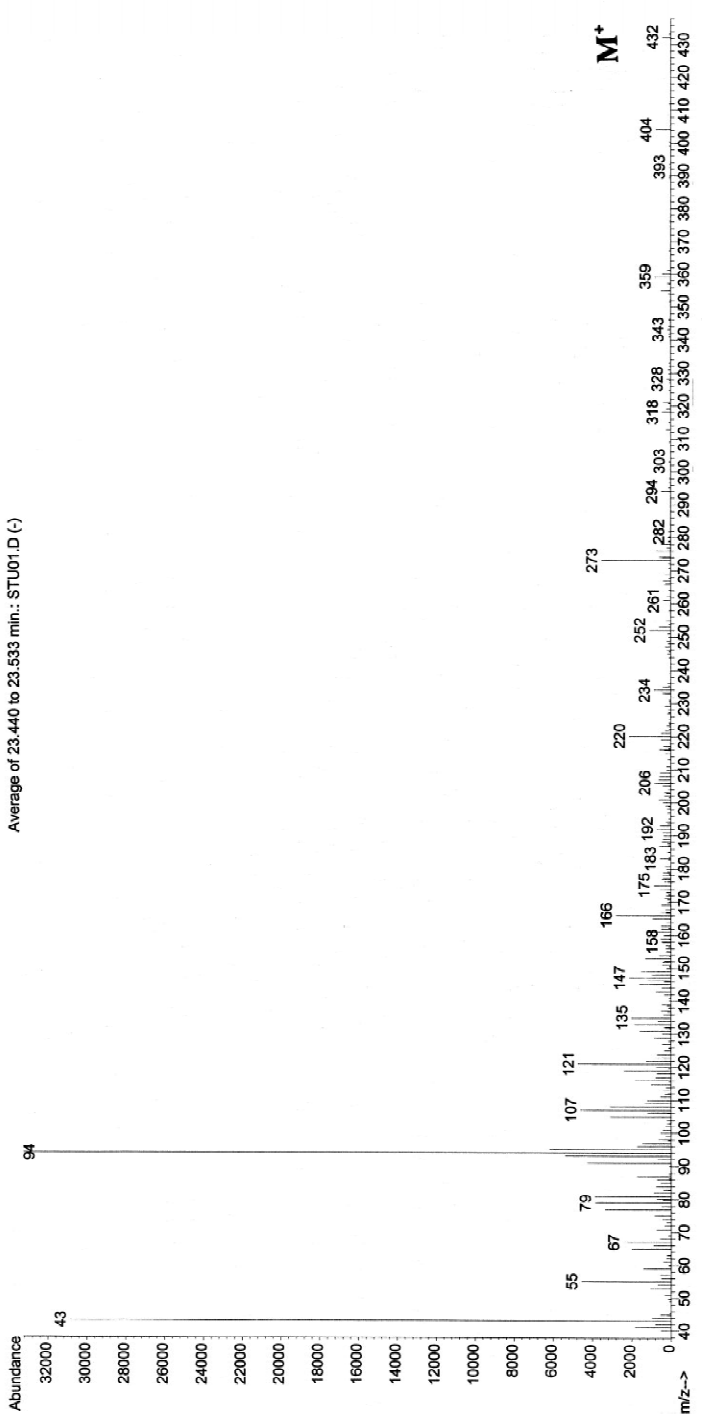

Fig. 3. The 70-eV mass spectrum of salvinorin A or divinorin A.

should contain significant amounts of the psychoactive acetylated salvinorin A molecule. A mass spectrum which could correspond to its desacetyl analog (salvinorin B) was detected in the methanolic extract only. Its putative molecular ion was $m/z=390$ and the majors ions occurred at $m/z=43$, 94 and 291.

Due to the lack of a commercially available authentic standard of salvinorin A, no quantification could be performed and the pharmacological activity of the seized plant could not be assessed.

Because salvinorin A has thus far been attributed uniquely to *S. divinorum* and that, as far as we know, no other natural source for this compound has been identified up to now nor synthetically produced, it was assumed that the unknown plant was *S. divinorum*.

4.1. Botanical identification

The dried plant was then compared and found to be identical to an authentic specimen of *S. divinorum* (G 340168) stored at the herbarium of the Conservatoire et Jardin Botaniques de la Ville de Genève, Switzerland. In particular, the specific characteristics of the stem and the typical morphology of the leaves confirmed that the specimens belonged to that species.

5. Discussion

Salvia divinorum is employed as a shamanic inebriant by the Mazatec Indians of the Mexican state of Oaxaca [3]. This plant is known from the Indians as the 'leaves of Mary, the Shepherdess'. They believe it allows them to travel to heaven and talk to God and the Saints about divination, diagnosis and healing [4]. Interesting enough, even though this species was known to the Mazatec Indians for several centuries, it was described only recently, in 1962 [3].

Both human and animal testing of salvinorin A indicated it had psychoactivity and potency similar to that of mescaline [4]. Vaporizing and inhaling 200–500 μg of pure salvinorin A induces profound hallucinations. Levels in leaves were found to range from 0.89 to 3.70 mg/g dry weight [5], a concentration which is very likely sufficient enough to induce psychoactive effects. In order to assess salvinorin A levels in plant organs, a reference standard was purified from *S. divinorum* leaf extracts and authenticated by NMR. Salvinorin A was quantified in plant tissues by reversed-phase high-performance liquid chromatography [5].

The leaves of *S. divinorum* are prepared in various manners for use as a psychotropic agent. The dried leaves may be smoked like marijuana joints. Traditionally, the fresh whole leaves are masticated and swallowed or, alternatively, the leaves are crushed to extract the juices which are then drunk [6]. The oral mucosa seems to play an essential role as an absorption site for salvinorin A from orally ingested leaves. The leaves may be crushed in water to prepare an infusion. Taken in small doses (4–5 pairs of fresh or dried leaves), the plant acts as a tonic or panacea as well as for magical healing. When prepared with large doses (20–60 pairs of fresh leaves), the infusion acts as a mild but

effective hallucinogen [7]. It was reported that ingestion of the infusion resulted in an astounding visual, oral/aural, and tactile hallucination [8]. Until recently, ignorance of drug addicts in the existence of this mint, its bitter taste, and a misunderstanding of its psychotropic effects have kept it from becoming a recreational drug. Nevertheless, it was reported that young people from Mexican cities travel to the Sierra Mazateca and purchase dried leaves of *S. divinorum* to make into cigarettes and smoke as a marijuana substitute. The effect is reportedly milder than that of *Cannabis* [5].

Since discovering this first specimen of *Salvia divinorum*, other plants have been found in the greenhouses of several horticulturists suggesting that interest for this mint is growing in Switzerland. Here it is important to point out that neither *S. divinorum* nor its active compound salvinorin A are listed in the Swiss narcotic law. In California and other parts of the US, it is reported to be employed as a legal hallucinogen [4].

Many web sites are dedicated to *S. divinorum*. For instance, data concerning the botany, ethnobotany, biochemistry and pharmacology of *S. divinorum* can be found on http://salvia.lycaeum.org/ott.html. Another relevant web site is http://sabia.com/salvia/.

6. Conclusions

In conclusion, forensic toxicologists are facing a growing amount of new psychotropic drugs, some of them are difficult to detect and quantify because no reference standard can be purchased and only scarce data are available about their metabolism, pharmacokinetic and toxicology. In this regard, *Salvia divinorum* and salvinorin A are good examples.

Acknowledgements

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