

# *Salvia Divinorum*

## *Effects, Legal Status and Analysis*

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When you need to know.™

# Salvia Divinorum

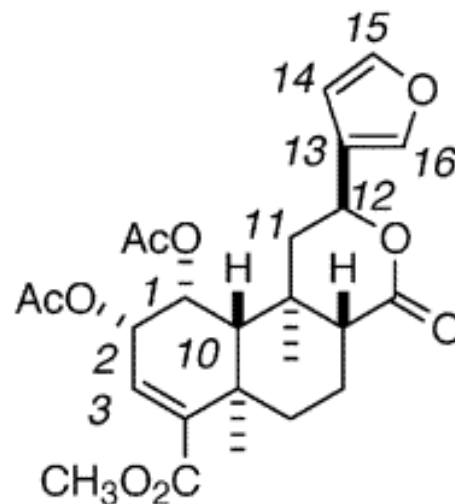
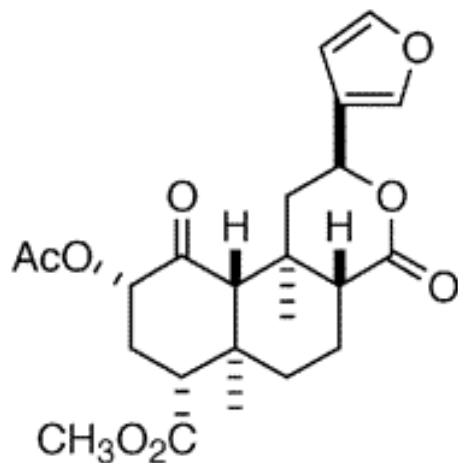
- Salvia; Sal; Magic Mint, Mystic Sage
- Ska Pastora; Sally-D; Diviners Sage; Shepherdess's Herb; ska Maria Pastora; hojas de Maria; yerba de Maria;
- “Salvia divinorum is a sprawling perennial herb found in the Sierra Mazatec region of Mexico. Its leaves contain the extremely potent Salvinorin A. It has a history of buccal use as a divinatory psychedelic, and has been widely available since the mid 1990s primarily as a smoked herb. Its effects are considered unpleasant by many people.”



<http://www.erowid.org/plants/salvia/salvia.shtml>

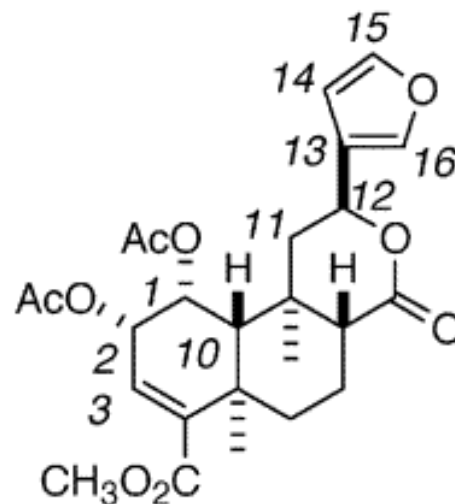
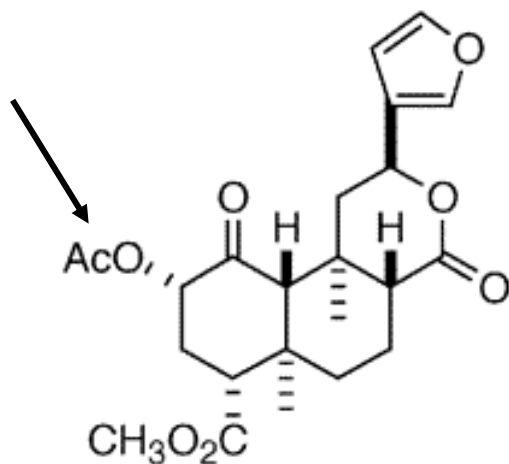
# Salvia Divinorum - Chemistry

- Active component – Salvinorin A
- Other natural products –
  - Salvinorin C-G, Divinatorins A-E, Salvinicin A-B
- Synthetic derivatives are under investigation for treatment of Alzheimers, Parkinsons, schizophrenia, and stimulant dependence.



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# Salvia Divinorum - Use

- Currently sold in head shops, tobacco shops, and online.
- SAMHSA estimates 750K – 1M last year use (2007).
- “Buy Salvia” Google search generates 285,000 hits.
- Available as plants, crushed leaves, extract
- Extracts contain Salvinorin A and B

(ug/mg)	Sal A	Sal B
Leaves	3.2 - 5.0	0.10 - 0.17
Extract	4.1 - 38.9	0.26 - 2.42



# Salvia Divinorum - Pharmacology

- Salvinorin A – potent Kappa Opioid Receptor agonist
- Kappa Receptor linked to analgesia, hallucinations.
- Binds butorphanol, nalbuphine, and pentazocine.
- No activity in 50 other receptors, transporters and ion channels.
- Non-nitrogenous



# Salvia Divinorum - Effects

- Following smoking, effects are intense but short lived.
- Psychedelic–like changes in visual perception.
- Mood and somatic changes
- Modified perception of external reality.
- Decreased ability to interact with self or surroundings



Gonzalez, et al, 2006

# Salvia Divinorum - Effects

Best Things		Worst Things		Unpleasant After-Effects	
The "Trip"	13	Duration	12	Tiredness	4
Happiness	9	Control	5	Heaviness	4
Dissociation	6	After-effects	4	Dizziness	3
Visual Effects	5	Physical fx	3	Exhaustion	3
Rapid onset	3	Intensity	2	Grogginess	1
Great potency	3			Mental slowness	1
Relaxation	2				



# Salvia Divinorum – Adverse Effects

- 37 Exposures to Salvia Divinorum
- Common co-ingestants: ethanol, MJ, mushrooms
- 18 to Salvia alone
- Most severe adverse effects from polydrug use.



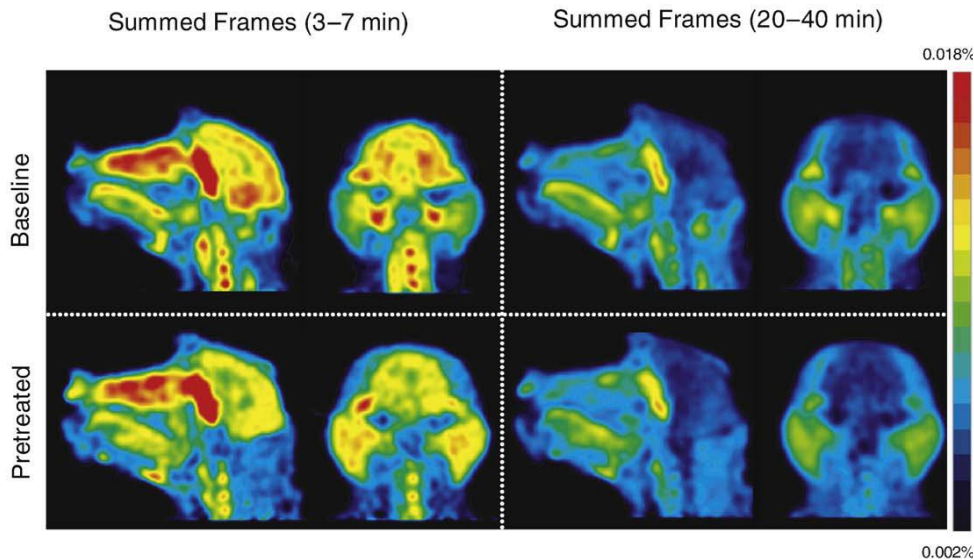
# Salvia Divinorum – Adverse Effects

<i>Clinical Feature</i>	<i>Frequency</i>
Altered Mental state	7
Hallucinations	3
Excessive laughter	1
Dizziness	1
Mydriasis	2
Flushing	3
Diaphoresis	1
Tachycardia	2
Palpitations	1
Hypoglycemia	1

•18 Isolated  
Salvia  
Exposures

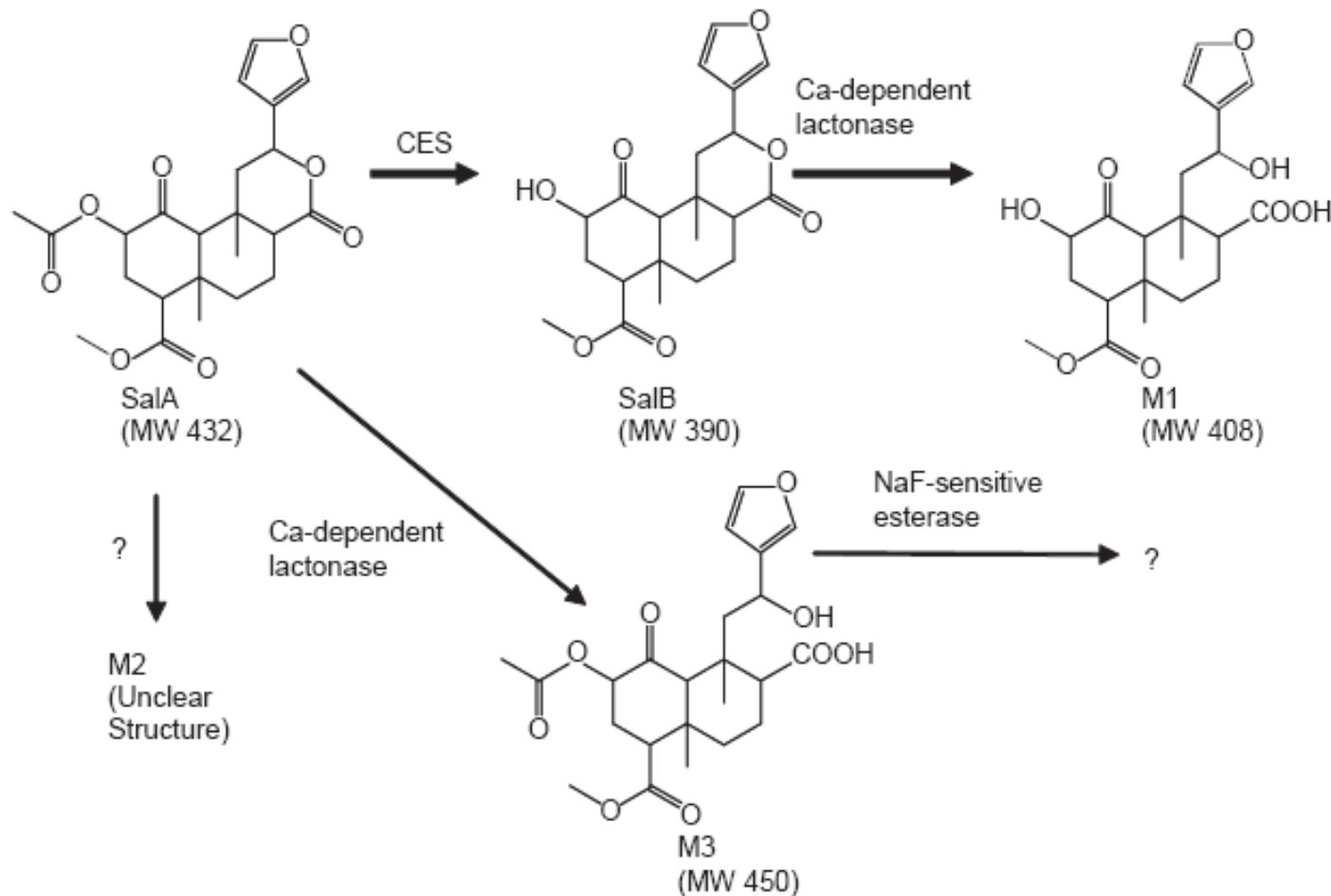
# Salvia Divinorum - Pharmacodynamics

- C<sup>11</sup> Salvinorin A administered to baboons (IV).
- Extremely rapid uptake
- Peak activity achieved in 40 seconds
- Represents 3.3% of dose
- PET kinetics match onset and dissipation in humans



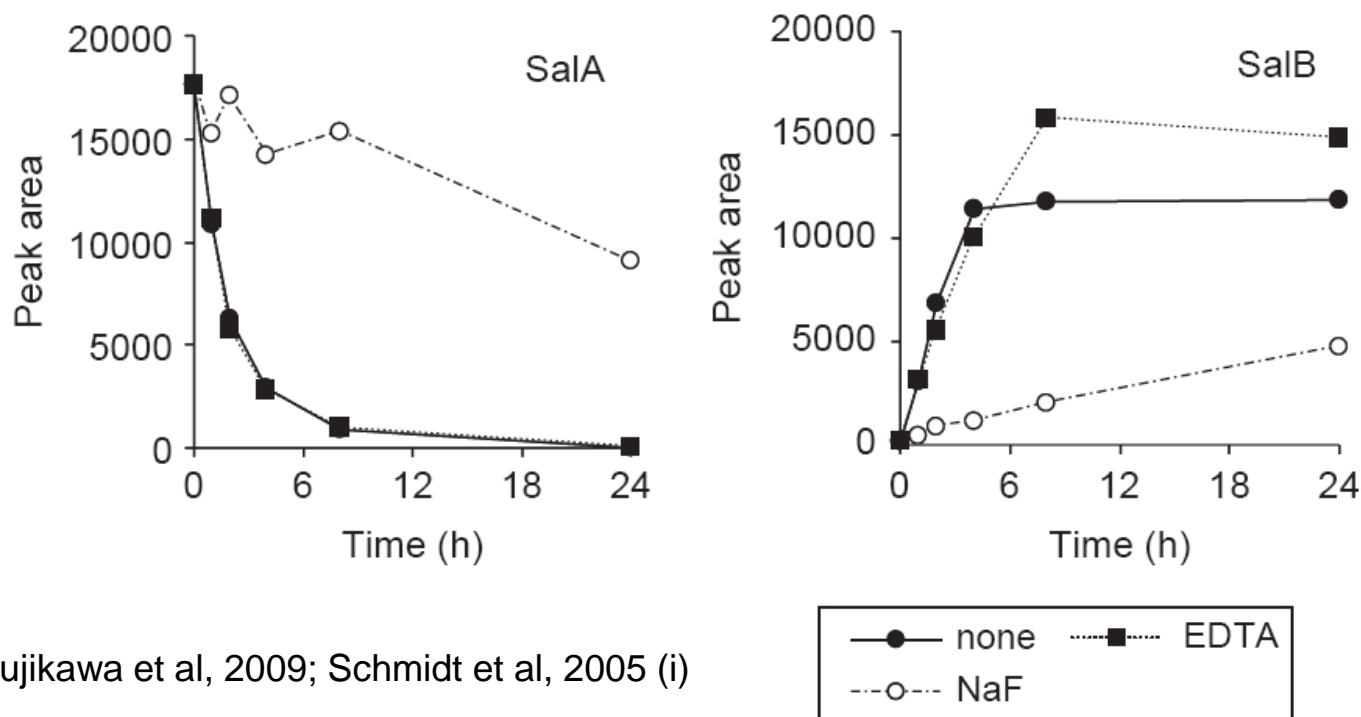
Hooker et al, 2008

# Salvia Divinorum - Metabolism



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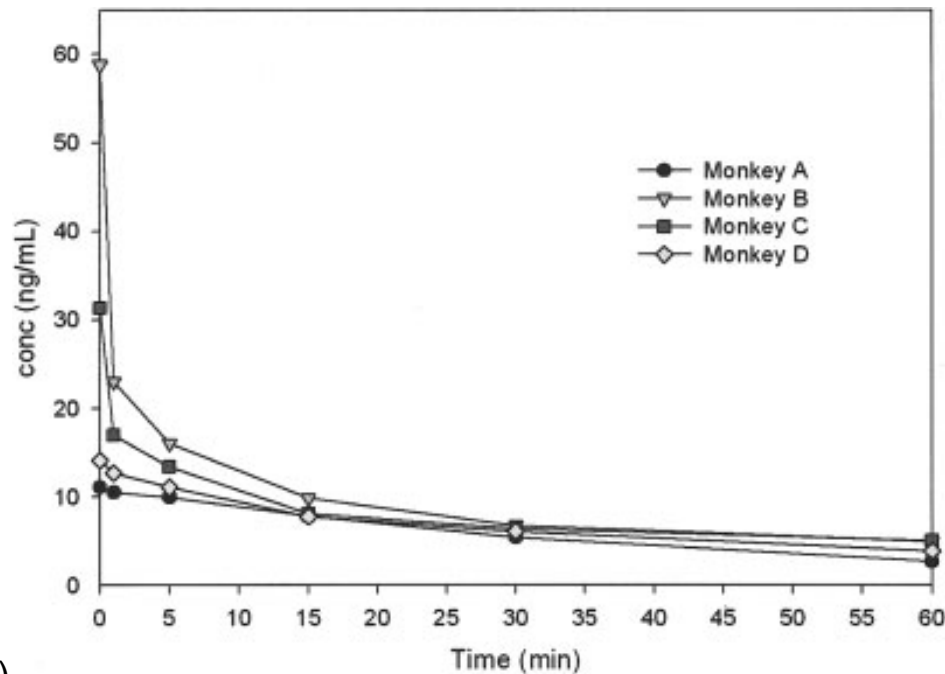
- Salvinorin A degrades to Salvinorin B in rat plasma, monkey blood.
- NaF but not EDTA inhibits conversion
- Implicates plasma carboxylesterase in conversion.



Tsujikawa et al, 2009; Schmidt et al, 2005 (i)

# Salvia Divinorum - Metabolism

- Salvinorin A (0.32mg/Kg) IV administration to Rhesus monkeys.
- Elimination half life 56 ( $\pm$ 24 mins)
- Salvinorin B never reached the limit of detection (50ng/mL).



Schmidt et al, 2005 (ii)

# Salvia Divinorum – Human Study

- Two subjects with prior experience with hallucinogens, smoked 75mg of salvia leaves, for three minutes, *ad lib.*
- Oral fluid collected at 1 hour post smoking.
- Urine collected at 0-1.5 hrs, and 1.5-9 hrs.
- Sweat patches applied and removed 2 hrs after smoking.
  
- *“Unfortunately... blood collection was not possible... both volunteers experienced intense hallucinations that started about 30 seconds after inhaling peaking at 3-5 minutes, and lasting about 15-20 minutes. During that period blood drawing was considered unsafe, and at the end of the experience the subjects refused blood drawing.”*

# Salvia Divinorum – Human Study

- Dose 0.58mg Salvinorin A administered.
- Only Salvinorin A measured

	Oral fluid (ng/mL)	Urine (ng/mL)		Sweat Patch
		0-1.5hrs	1.5-9.5hrs	
	1 hr			2 hrs
Sub 1	25.0	10.9	N.D.	N.D.
Sub 2	11.1	2.4	N.D.	N.D.



# Scheduling Status of Salvia by State

CA	Prohibit sales to minors
DE	Schedule I
FL	Schedule I
KS	Schedule I
IL	Schedule I
LA	Schedule I
MN	Prohibit sales to minors
MS	Schedule I
MO	Schedule I
NE	Schedule I
NC	Schedule I
ND	Schedule I
OK	Schedule I
SD	Class 1 Misdem/Class 6 Felony
TN	Class A Misdemeanor
VA	Schedule I

Pending legislation in:  
IN, IA, MD, MA, NJ, NY, OH, PA,  
TX, UT



# Sentinel Forensic Case

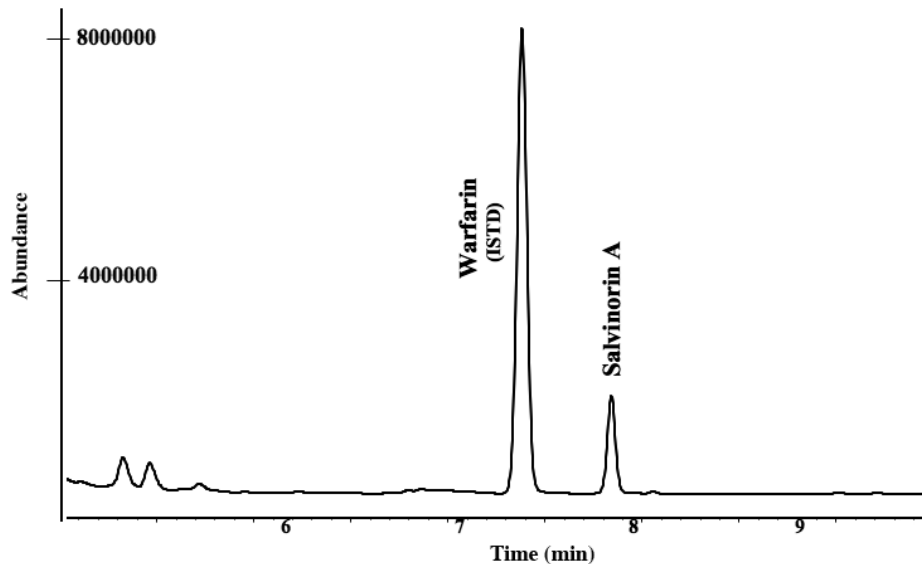
- Delaware teen, Brett Chidester committed suicide, aged 17, in 2006.
- ‘Ethnosupply’—a Canadian based Internet company allegedly sold Salvia Divinorum to Chidester some four months before his death.
- Chidester wrote notes including “*How can I go on living after I learned the secrets of life, It took me 17 years, but I finally figured it out. I can't tell you that here because that kind of information can cause chaos.*” in apparent reference to revelations he experienced after taking salvia.
- His parents successfully campaigned to outlaw salvia in DE in 2006.

# Salvinorin Analysis

- GCMS/EI/SIM reported for Salvinorin A
  - Pichini et al., 2005
  - $\alpha$ -methyltestosterone ISTD
  - LOD 5ng/mL, LOQ 15ng/mL
  - Validated for sweat, blood, urine, oral fluid.
- LCMS/APCI reported for Salvinorin A and B
  - Schmidt, et al, 2005
  - CD<sub>3</sub> labelled Salvinorin A ISTD
  - Sal A, LOQ 2ng/mL; Sal B LOQ 50ng/mL

# Salvinorin Analysis

- LCMS/ESI reported for Salvinorin A
  - McDonaugh et al, 2008
  - Warfarin ISTD
  - Sal A, LOD 2.5ng/mL; LOQ 5ng/mL



# NMS Labs - Salvinorin Analysis

- Positive ion electrospray liquid chromatography tandem mass spectrometry (LC-MS/MS).
- Blood, urine, plasma
- Single step L/L extraction

Analyte	MRM	MRM	RT (min)
Sal A	433/373	433/295	6.67
Sal A-d3	436/376	N/A	6.67
Sal B	389/313	389/295	5.88



[Test requirements available at www.nmslabs.com](http://www.nmslabs.com)

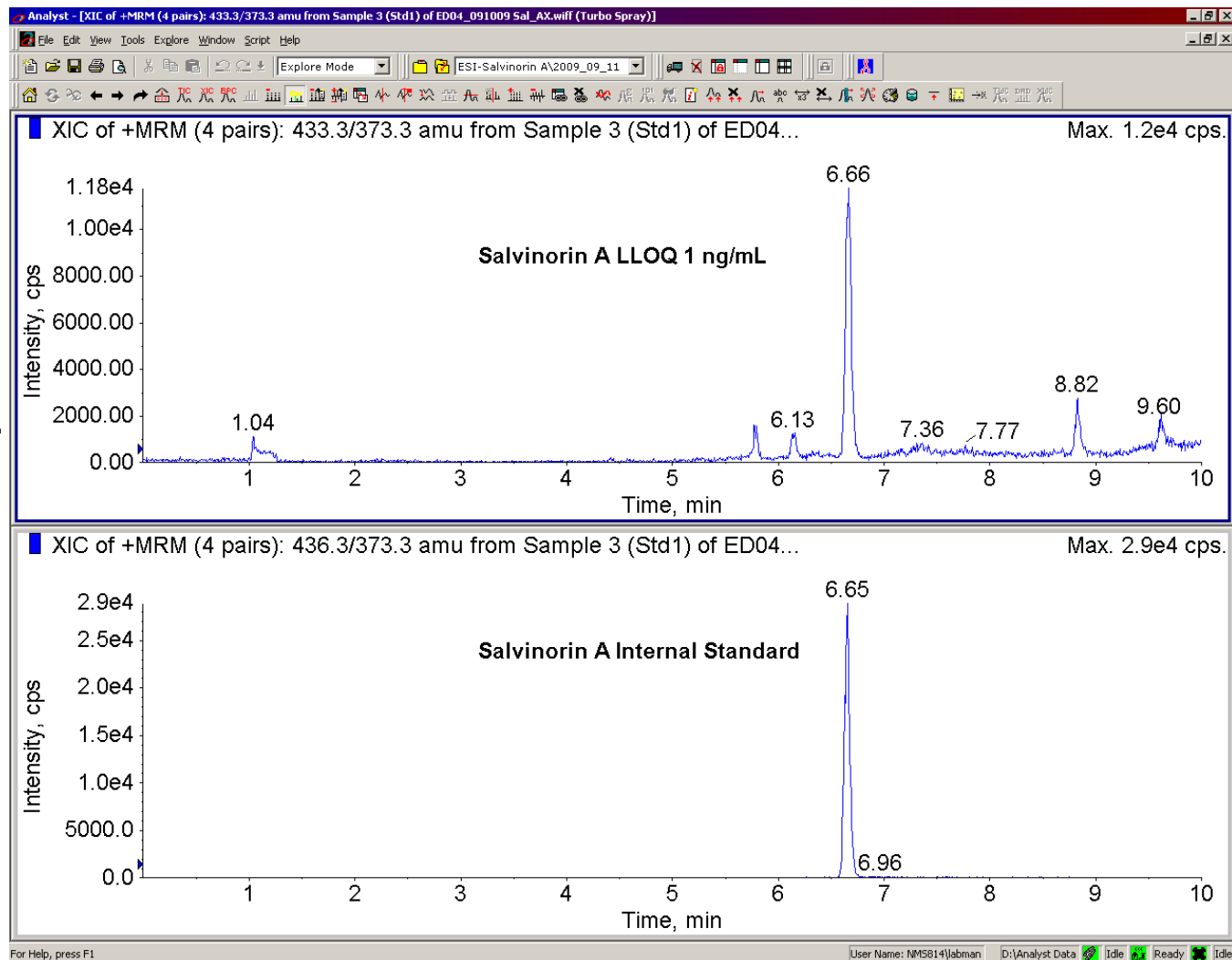
# LCMS/MS Salvinorin Analysis

- Assay Validation
  - Within run/between run precision
  - Recovery
  - Matrix stability
  - Autosampler stability
  - Prep stability
  - Dilution stability
  - Matrix matching
  - Interference
  - Freeze thaw
  - Carryover



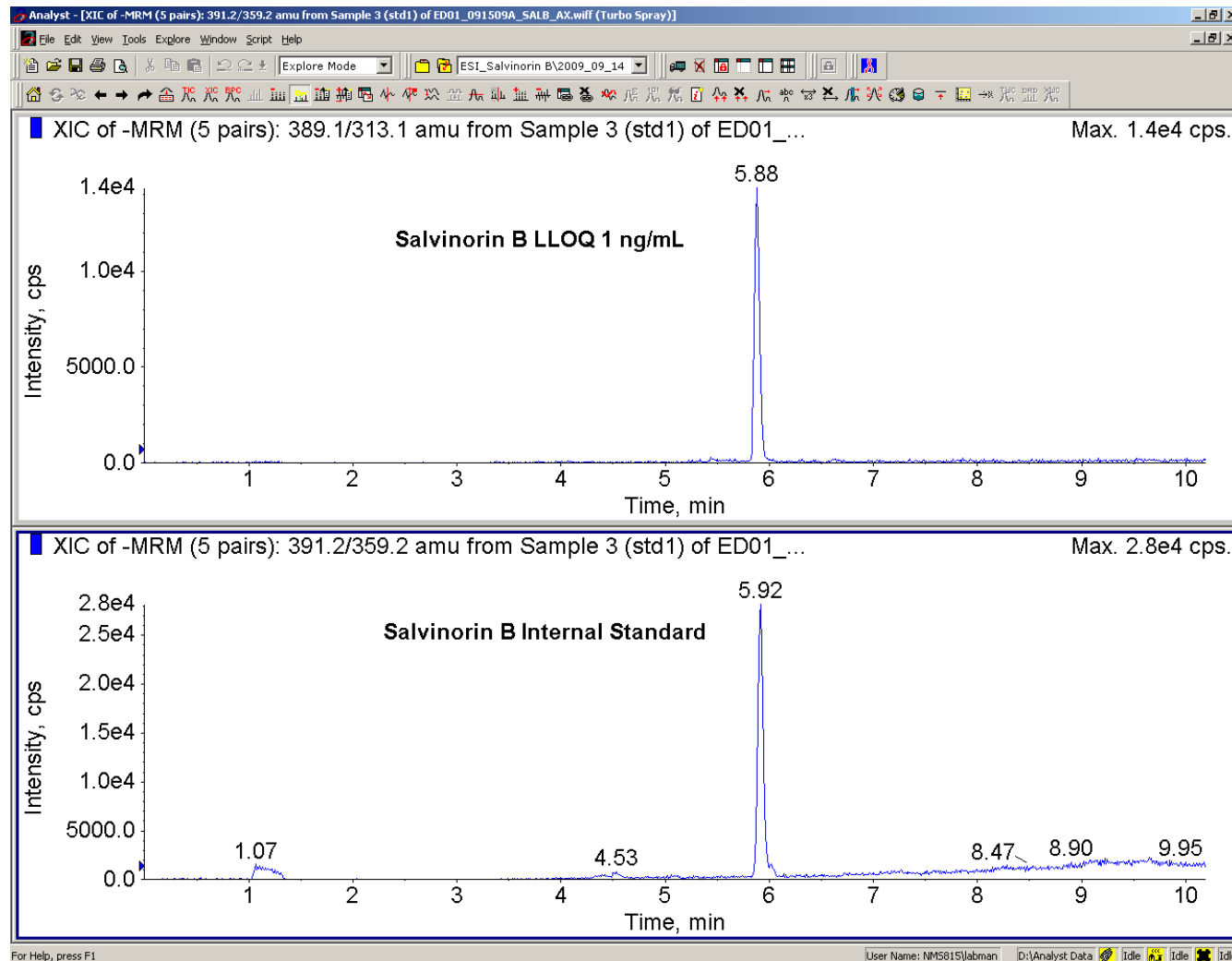
# NMS Labs - Salvinorin A Analysis

- Sal A
- LOQ
  - 1ng/mL
- LOD
  - ~0.25ng/mL



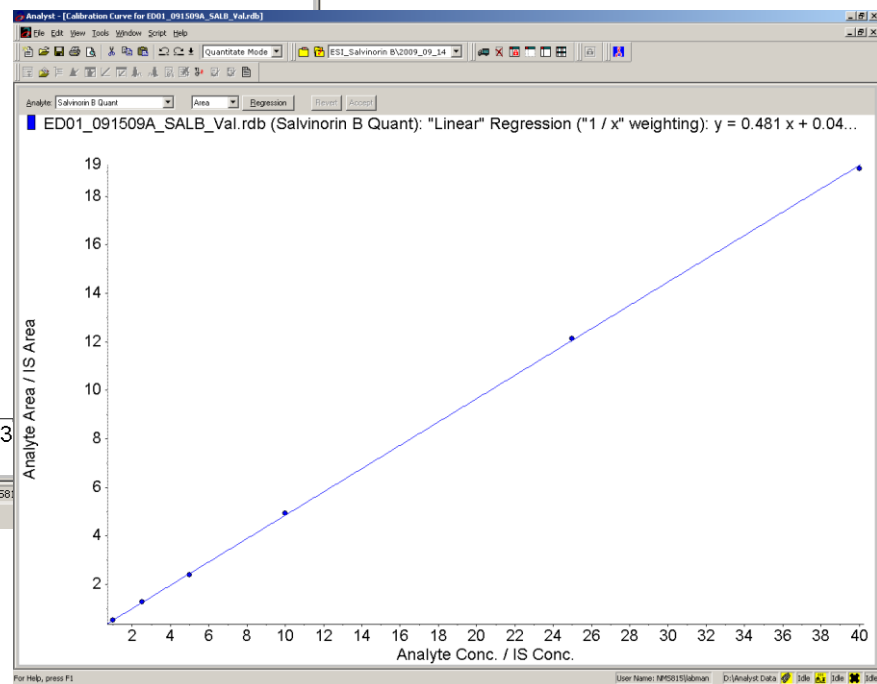
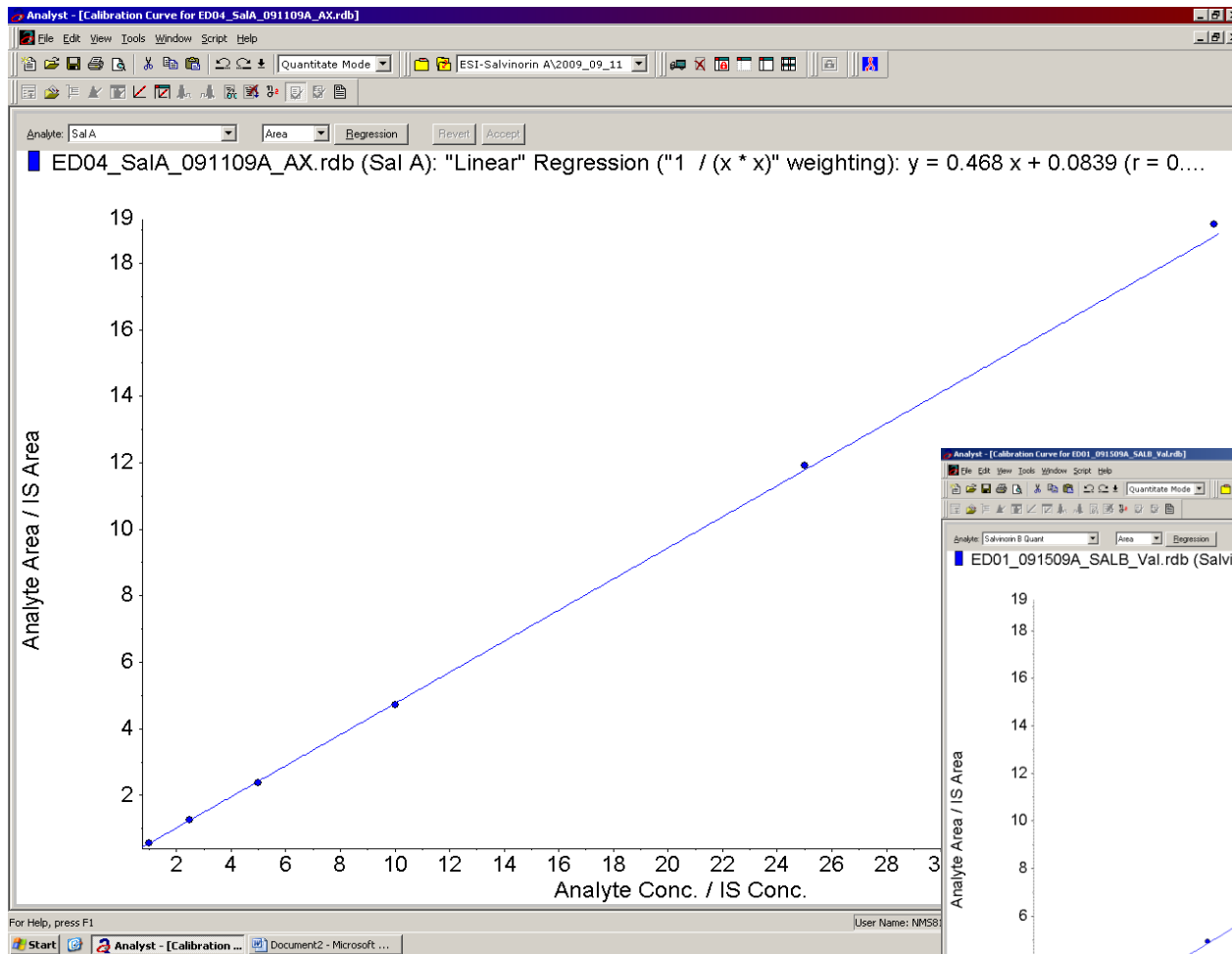
# NMS Labs – Salvinatorin B Analysis

- Sal B
- LOQ
  - 1ng/mL
- LOD
  - ~0.25ng/mL





# LCMS/MS Salvinorin Analysis



# Salvinorin A and B – Stability

Days	1	2	9	14	28
Blood NaF 25°C	N/Y	N/Y	N/Y	N	N
Blood NaF 4°C	N/Y	N/Y	N/Y	N	N
Blood NaF -20°C	Y	Y	Y	Y	Y
Plasma NaF 25°C	Y	Y	Y	Y	N
Plasma NaF 4°C	Y	Y	Y	Y	Y
Plasma NaF -20°C	Y	Y	Y	Y	Y
Urine* 25°C	Y	Y	N/Y	N	N
Urine* 4°C	Y	Y	Y	Y	Y
Urine* -20°C	Y	Y	Y	Y	Y

\* unpreserved

# Salvia – Forensic Concerns

- Salvia is a potent, readily available, difficult to control hallucinogen/dissociative.
- It is openly on sale, in many states and on the internet.
- Adverse effects on human performance.
- General concerns regarding intoxicants.
- Unknown residual effects.
- Use in prohibited populations.



# Unanswered questions

- Legal future of Salvia – Federal or State by State?
- Duration of effect and hangover.
- Detection window.
- Longer lived markers – M1, M3?
- Need for a sensitive screening method for Salvinorin A and B

# Acknowledgements

- Lab
  - Allan Xu
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  - Amanda Panepinto
  - Julie Ruth

- Join Forensic Toxicology on [www.Linkedin.com](http://www.Linkedin.com)

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