

Ayahuasca



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The Case

- 40 year old female on a weekend ayahuasca retreat
- No PMH or FH of mental health issues
- History of cannabis use in years prior, single use of MDMA
- Consumed ayahuasca twice during the retreat

After Effects

- Consumed ayahuasca on a Friday with no obvious issues
- Normal behavior and activity throughout Saturday
- “Incoherent discourse” shortly before ingestion on Sunday
- Paranoia/delusions occurred 15-20 minutes after ingestion
- Remained in this state for the next 24 hours

Ayahuasca

- Similar usage to many other topics previously discussed
 - Often part of religious or healing ceremonies
- Primarily used in South American/Amazonian groups
 - Unclear when ayahuasca use began widespread in the region
- Term may compromise multiple different recipes
 - Typically made from a combination of botanicals
 - Generally a recurring combination of two particular agents
 - Variations are often region specific

Making Ayahuasca

- *Banisteriopsis caapi*
- Often *Psychotria viridis*
- Components boiled together or separately
- Often boiled in water until water is significantly reduced
 - May take hours and occur over a couple of days



What is Really Happening?

- *Psychotria viridis* contains, among many things, DMT
 - Dimethyltryptamine
- DMT a hallucinogenic similar to LSD, psilocybin
 - 5-MeO-DMT an active component of Colorado River Toad toxin
- Action likely mediated by 5-HT_{2A} agonist activity
- Not particularly orally active
 - Rapidly broken down by monoamine oxidase

Key Piece of Ayahuasca's Effects

- *Banisteriopsis caapi* contains 3 critical components:
 - Harmine
 - Harmaline
 - Tetrahydroharmine
- These β -carbolines function as MAO inhibitors
- Presence enables oral activity of DMT
- In high enough doses are themselves psychoactive

Adverse Effects

Table 2. Frequency of participants' reported adverse physical effects (n = 8,216).

	Total sample (8,216)	Single ayahuasca use participants (598)
	n %	n (%)
Adverse physical effect^{1,2}	5,742 (69.9)	334 (55.9)
General symptom adverse effect^{1,3}	5,603 (68.2)	321 (53.7)
Vomiting/nausea	5,097 (62.0)	281 (47.0)
Headache	1,460 (17.8)	57 (9.5)
Abdominal pain	1,052 (12.8)	31 (5.2)
Breathing difficulties	599 (7.3)	33 (5.5)
Chest pains	384 (4.7)	14 (2.3)
Arthromyalgical adverse effect^{1,4}	883 (10.7)	39 (6.5)
Aching muscles	617 (7.5)	29 (4.8)
Coughing/wheezing	273 (3.3)	5 (0.8)
Stiff/swollen joints	182 (2.2)	12 (2.0)
Neurological adverse effect^{1,5}	416 (5.1)	20 (3.3)
Fainting	335 (4.1)	13 (2.2)
Fits or seizures	106 (1.3)	7 (1.2)

¹ Reported presence of some of the adverse physical effects studied

² adverse physical effects range (0–10) and median (1.0)

³ adverse psychophysical effects range (0–5) and median (1.0)

⁴ adverse arthromyalgic effects range (0–3) and median (0.0)

⁵ adverse neurological effects range (0–2) and median (0.0).

Duration of Activity and Persistence

- Ayahuasca's effects are classically recognized as:
 - Beginning within 30 minutes
 - Peak sometime between 1-2 hours
 - Persist for up to 4-6 hours
- Most mental health symptoms resolved within one week
- In one study, ~12% reported needing professional support
- No apparent development of tachyphylaxis or dependence

Reported Adverse Mental Effects

Table 3. Frequency of participants' reported adverse mental health effects.

	Total sample (7,839)			Single ayahuasca use participants (565)
	Adverse effects	Adverse effects duration	Severe adverse effects	Adverse effects
	n (%)	n (%)*	n (%)	n (%)
Adverse mental health effects^{1,2}	4,341 (55.4)			289 (51.2)
Emotional-cognitive adverse effects^{1,3}	3,293 (42.0)			243 (43.0)
Feeling disconnected or alone	1,650 (21.0)	788 (49.0)	233 (3.0)	120 (21.2)
Nightmares, disturbing thoughts, feelings, or sensations	1,506 (19.2)	611 (52.7)	175 (2.2)	88 (15.6)
Feeling nervous, anxious, or on edge	1,483 (18.9)	833 (57.2)	247 (3.2)	110 (19.5)
Feeling down, depressed, or hopeless	1,300 (16.6)	643 (50.6)	149 (1.9)	79 (14.0)
Not being able to stop or control worrying	1,201 (15.3)	665 (56.7)	185 (2.4)	85 (15.0)
Little interest or pleasure in doing things	1,160 (14.8)	595 (52.3)	134 (1.7)	76 (13.5)
Difficulty knowing what is real and not real	1,011 (12.9)	509 (51.8)	167 (2.1)	84 (14.9)
Altered perception adverse effects^{1,4}	3,004 (38.3)			159 (28.1)
Hearing or seeing things that other people do not hear or see	2,236 (28.5)	646 (44.1)	251 (3.2)	76 (13.5)
Feeling "energetically attacked" or a harmful connection with a "spirit world"	1,186 (14.9)	579 (48.9)	191 (2.4)	49 (8.7)
Visual distortions	2,236 (15.1)	1330 (60.7)	342 (4.4)	117(20.7)

* Calculated for those who had been reported Adverse Effects. Missing data not included

¹ reported presence of some of the adverse mental health effects studied

² adverse mental health effects total score mean (12.78), S.D. (4.3) and range (0–30)

³ adverse emotional effects total score mean (1.76), S.D. (3.3), range (0–21)

⁴ adverse altered perception effects mean (1.02), S.D. (1.7), range (0–9).

Possible Risk Factors for Adverse Events

Table 4. History of ayahuasca use and medical status variables' relationships with the presence of adverse physical effects.

	F062	<i>p</i>	OR	OR (95% C.I.)	
Age of initial use	.030	< .001	1.03	1.02	1.04
Doses/year	-.138	.04	.87	.76	.99
Lifetime use	.226	< .001	1.25	1.18	1.41
Last year use	.090	.05	1.09	1.00	1.20
Anxiety disorder	.187	.06	1.20	.99	1.47
Depressive disorder	.023	.80	1.02	.86	1.22
Substance use disorder	.239	.05	1.27	1.00	1.61
Alcohol use disorder	-.026	.82	.97	.78	1.22
Physical health conditions	.167	.002	1.18	1.06	1.32
Acute spiritual experience	.003	.17	1.00	1.00	1.01
Context					
Religious context	–	–	1		
Traditional shaman context	-.170	.11	.84	.68	1.04
Non-traditional context	-.041	.68	.96	.79	1.17
Non-supervised context	.374	.03	1.45	1.04	2.02

¹ Significant controlled variables: female: $\beta = .242$; $p < .001$; OR=1.27 (1.12-1.44); age at survey day: $\beta = -.033$; $p < .001$; OR=.97 (.95-.98); education: Diploma/advance diploma $\beta = .45$; $p = .05$; OR=1.57 (1.01-2.47); undergraduate/Bachelor $\beta = .63$; $p = .005$; OR=1.88 (1.21-2.92); Master's degree: $\beta = .71$; $p = .002$; OR=2.03 (1.30-3.15); PhD degree: $\beta = 1.05$; $p < .001$; OR=2.86 (1.69-4.85).

Fatalities

- Appears to be particularly rare though details are scarce
- Concerns around individuals with:
 - Cardiac issues
 - Other substance use
 - Drug/drug interactions
- One case linked to an allergic reaction
- Another to overdose

Ayahuasca Adverse Management


- Most likely will relate to psychoses
- Management can be complicated by use of other substances
- Benzodiazepines for acute agitation if appropriate
- Antipsychotic use (quetiapine, olanzapine, risperidone)
- 2-3 months or more typical for chronic management

In the News

Federal Settlement Will Allow Arizona Church To Import, Process And Use Ayahuasca As Religious Sacrament



Published on April 24, 2024

By **Ben Adlin** 

Case Conclusion

- Psychologist attending the retreat recommended risperidone 2 mg
- Symptoms resolved within 30 minutes
- Following 48 hours of being awake, slept for 7 hours
- Upon waking, psychotic symptoms had returned
- Admitted to hospital after 2 days and treated with haloperidol
- Ongoing treatment x 2 months without return of symptoms

Summary

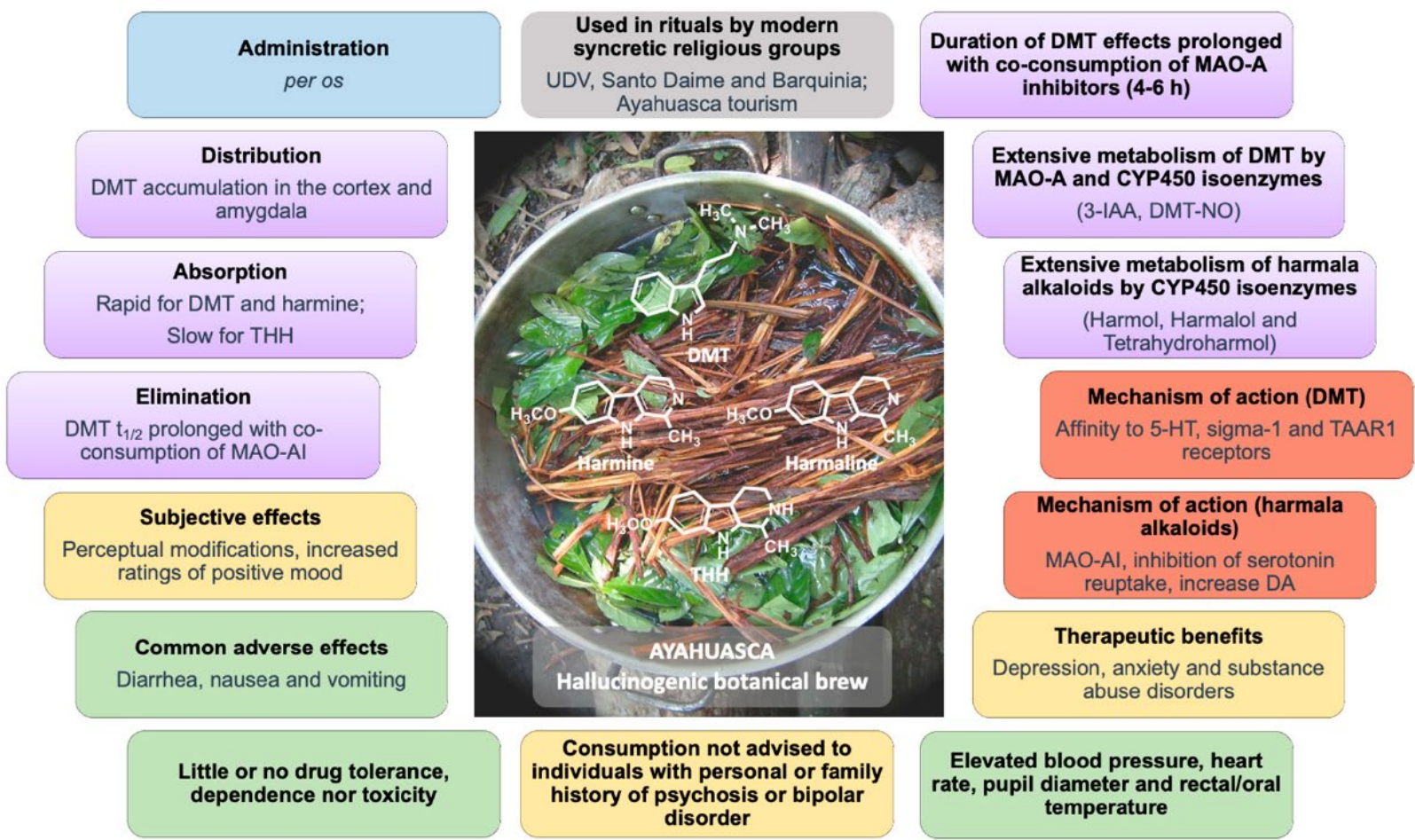


Figure 6. Pharmacokinetic and pharmacodynamic aspects of ayahuasca. 3-IAA: 3-Indole-acetic acid; 5-HT: Serotonin; DA: Dopamine; DMT: *N,N*-Dimethyltryptamine; DMT-NO: DMT-*N*-oxide; MAO: Monoamine oxidase; TAAR1: Trace amine-associated receptor type 1; THH: Tetrahydroharmine, UDV: *União do Vegetal*.

Conclusion

- Ayahuasca a unique combination of pharmacological agents
- Various formulations with different potencies/properties
- As with other hallucinogens, potential interest in therapeutic use
- Significant serious adverse effects most likely to be psychological
- If use is suspected, consider concomitant medication use