19e Congrès International d'Addictologie de l'ALBATROS

Investigation of Ayahuasca and Ibogaine in the Treatment of Alcohol Use Disorders in Brazil

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What is ayahuasca?

Ayahuasca and Culture

- Used for ritual and therapeutic purposes by Amazonian indigenous groups and syncretic religions (*Santo Daime, União do Vegetal*).
- Ritual use is legal in Peru, Colombia, Ecuador and Brazil.
- Present in at least 23 countries (~20.000 ritual users).

Source: personal archive; santodaime.org.

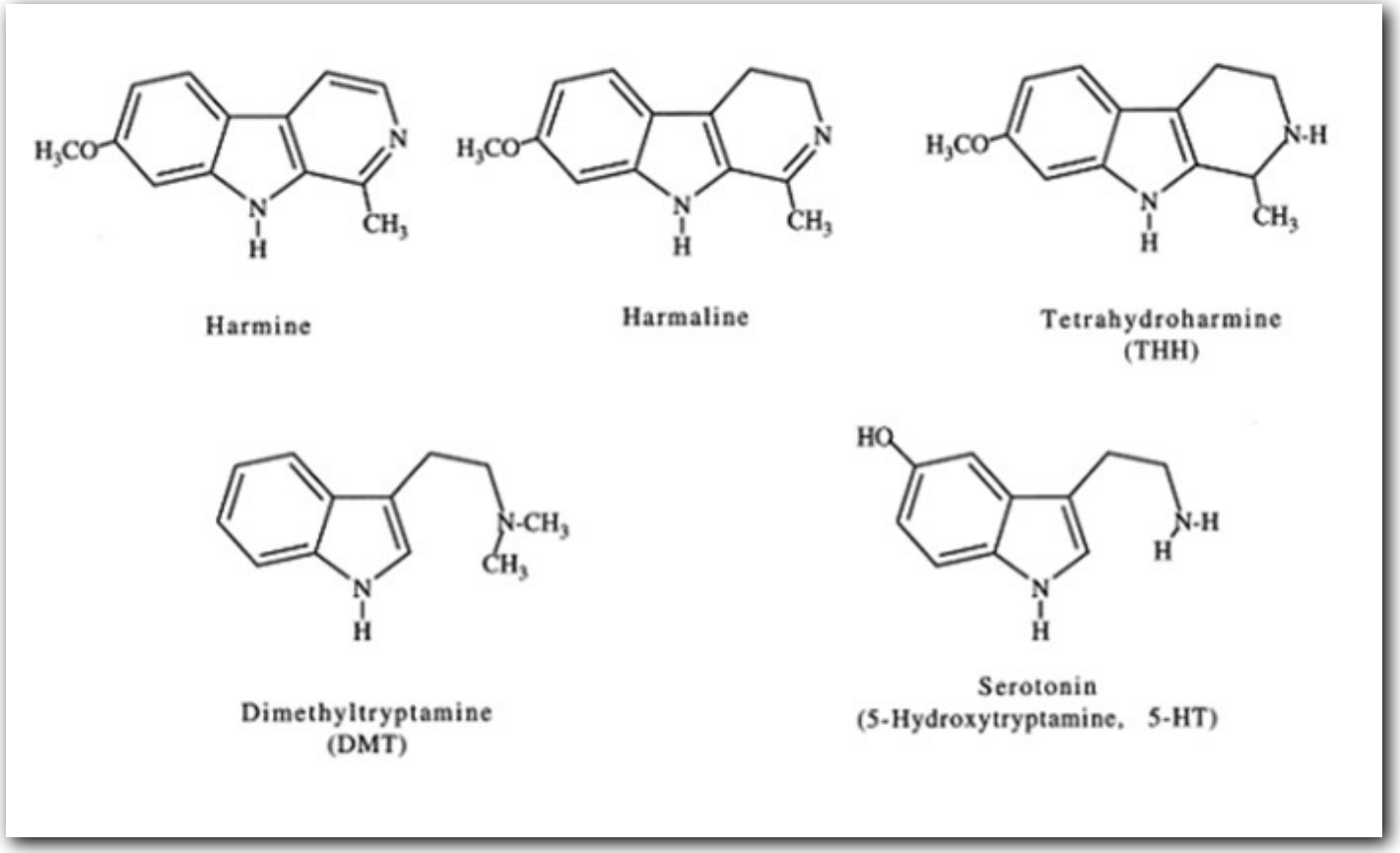
Ayahuasca and Botany

- ‘Ayahuasca’ refers to the *Banisteriopsis caapi* vine.
  - The word ‘ayahuasca’ comes from the Quichua: *aya* - spirit, *huasca* – liana/vine.
- The liana is used with several other plants, mainly *Psychotria viridis* and *Diplopterys cabrerana*.

Source: Giordano Rossi.

Ayahuasca Alkaloids

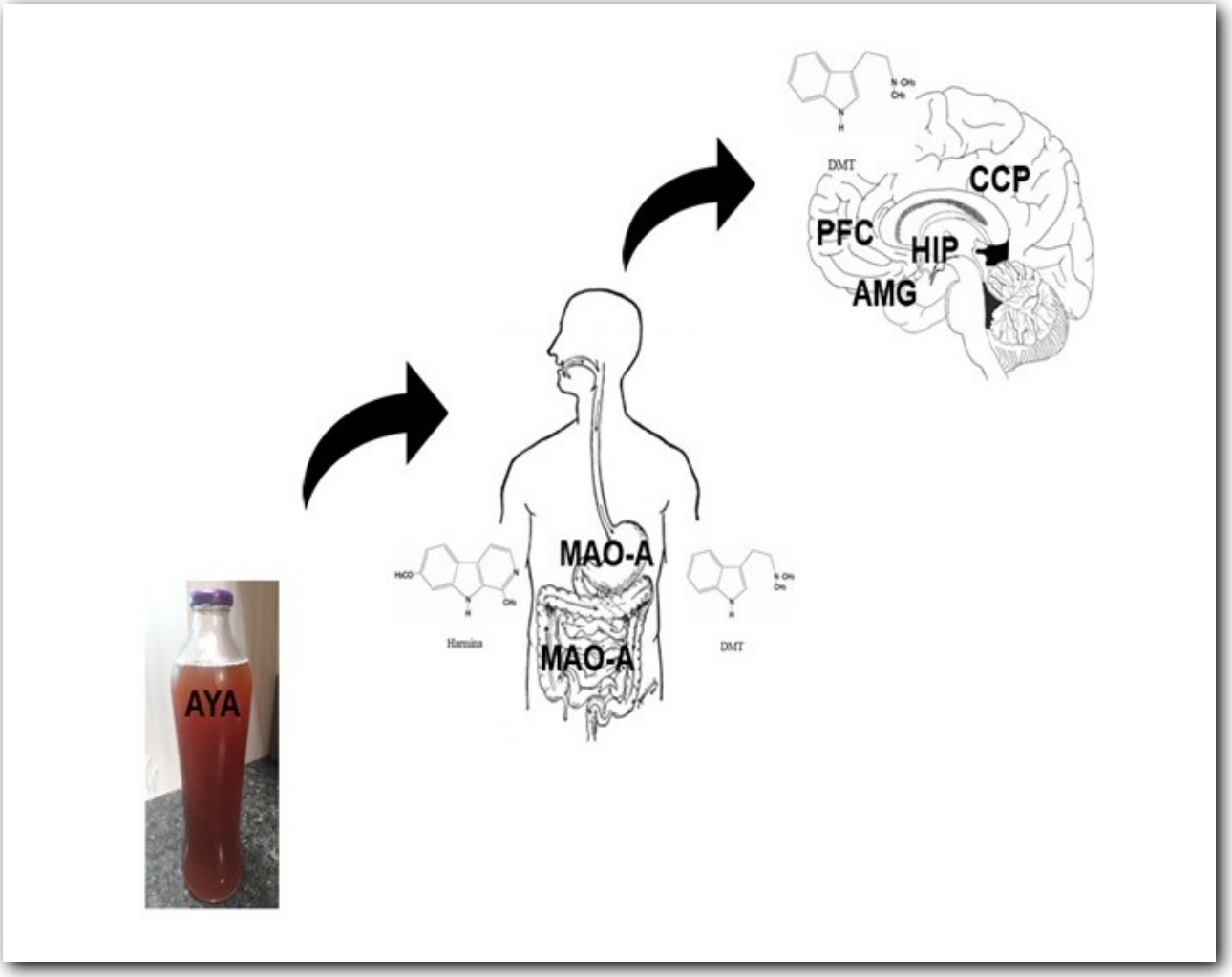
- *Banisteriopsis caapi* is rich in beta-carbolines.
- *Psychotria viridis* contains dimethyltryptamine (DMT).
- These compounds share their chemical structure with serotonin (5-HT).



Source: personal archive.

Ayahuasca Alkaloids

- DMT is orally inactive due to degradation by monoamine oxidase type A (MAO-A).
- In ayahuasca (AYA), the beta-carbolines inhibit MAO-A.
- Thus, DMT reaches systemic circulation and the brain: prefrontal cortex (PFC), hippocampus (HIP), amygdala (AMG), posterior cingulate cortex (CCP).

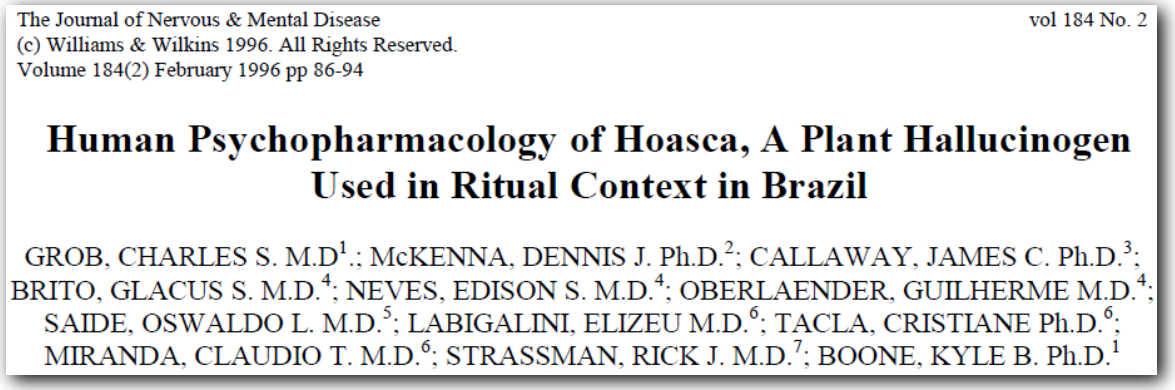


Source: Dos Santos & Hallak, 2019.

What are the effects of ayahuasca on drug use?

Observational studies

- No evidence of deleterious psychosocial effects typically caused by drugs of abuse in long-term rituals users, compared with non-users/controls.
- Less use of alcohol, stimulants and tobacco, compared to non-users/controls.



The Journal of Nervous & Mental Disease vol 184 No. 2

Volume 184(2) February 1996 pp 86-94

Human Psychopharmacology of Hoasca, A Plant Hallucinogen Used in Ritual Context in Brazil

GROB, CHARLES S. M.D[1].; McKENNA, DENNIS J. Ph.D.[2]; CALLAWAY, JAMES C. Ph.D.[3]; BRITO, GLACUS S. M.D.[4]; NEVES, EDISON S. M.D.[4]; OBERLAENDER, GUILHERME M.D.[4]; SAIDE, OSWALDO L. M.D.[5]; LABIGALINI, ELIZEU M.D.[6]; TACLA, CRISTIANE Ph.D.[6]; MIRANDA, CLAUDIO T. M.D.[6]; STRASSMAN, RICK J. M.D.[7]; BOONE, KYLE B. Ph.D.[1]

Drug and Alcohol Dependence 111 (2010) 257–261

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

comentário

ELSEVIER

Short communication

Assessment of addiction severity among ritual users of ayahuasca☆

Josep Maria Fábregas[a], Débora González[a], Sabela Fondevila[b], Marta Cutchet[a], Xavier Fernández[c], Paulo César Ribeiro Barbosa[d], Miguel Ángel Alcázar-Córcoles[e], Manel J. Barbanoj[g,h], Jordi Riba[f,g,h], José Carlos Bouso[f,g,*]

Source: Grob et al., 1996; Bouso et al., 2012.

Preclinical studies

- Reductions in alcohol, morphine, cocaine, and amphetamine self-administration.
- Reductions in amphetamine- and alcohol-induced conditioned place preference.

JOURNAL OF PSYCHOACTIVE DRUGS 2016

Effects of Ayahuasca and its Alkaloids on Drug Dependence: A Systematic Literature Review of Quantitative Studies in Animals and Humans

Amanda A. Nunes, B.Sc.[a], Rafael G. dos Santos, Ph.D. [b,c], Flávia L. Osório, Ph.D.[d,e], Rafael F. Sanches, Ph.D.[f], José Alexandre S. Crippa, Ph.D.[g,h], and Jaime E. C. Hallak, Ph.D.[g,h]

European Archives of Psychiatry and Clinical Neuroscience

Effects of ayahuasca and its alkaloids on substance use disorders: an updated (2016–2020) systematic review of preclinical and human studies

Lucas Silva Rodrigues[1] · Giordano Novak Rossi[1] · Juliana Mendes Rocha[1] · Flávia L Osório[1,2] · José Carlos Bouso[1,3,4] · Jaime E. Cecílio Hallak[1,2] · Rafael G. dos Santos[1,2,3]

Source: Nunes et al., 2016; Rodrigues et al. 2022.

Clinical studies

- Single dose of ayahuasca (0.7 mg/kg DMT) in university students with harmful alcohol use.
- Single-blind (n = 11).
- Ayahuasca was well tolerated:
  - Disorientation (90.91%)
  - Nausea (81.82%)
  - Gastrointestinal discomfort (81.82%)
- No serious adverse effects.
- Reductions in weekly alcohol use.

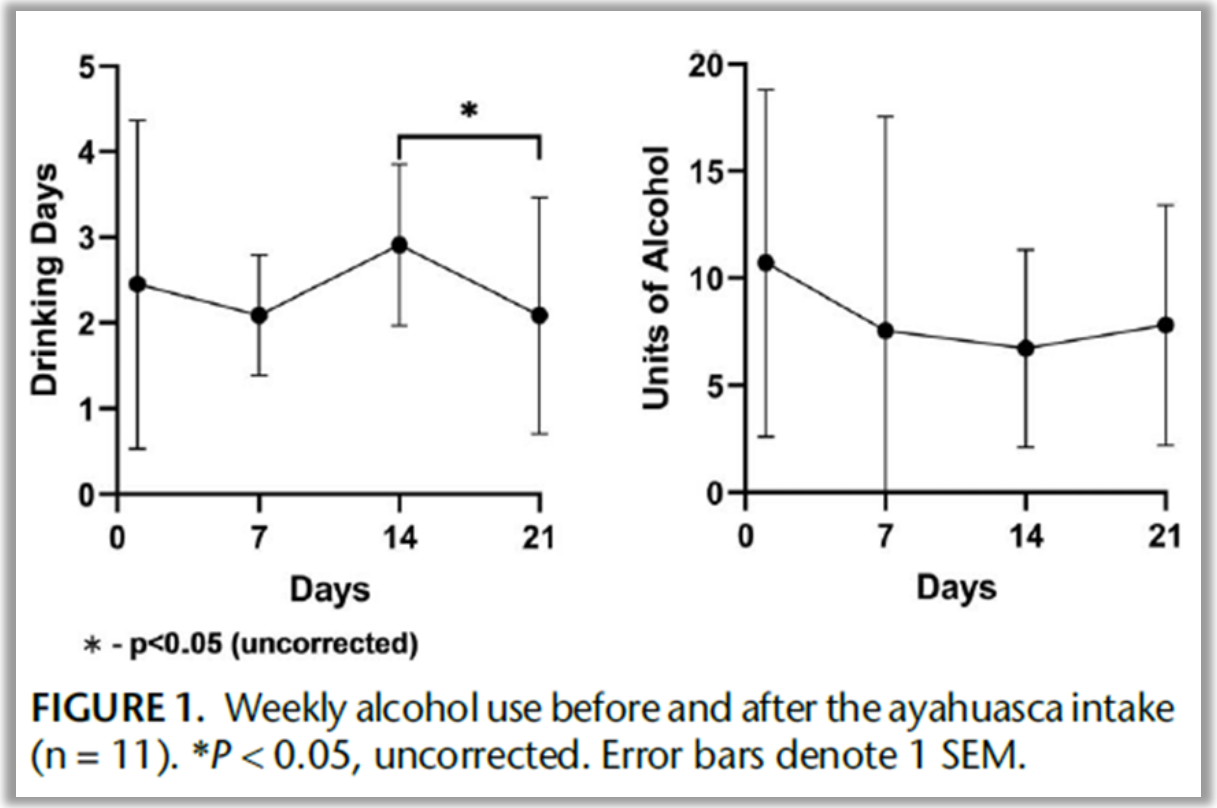


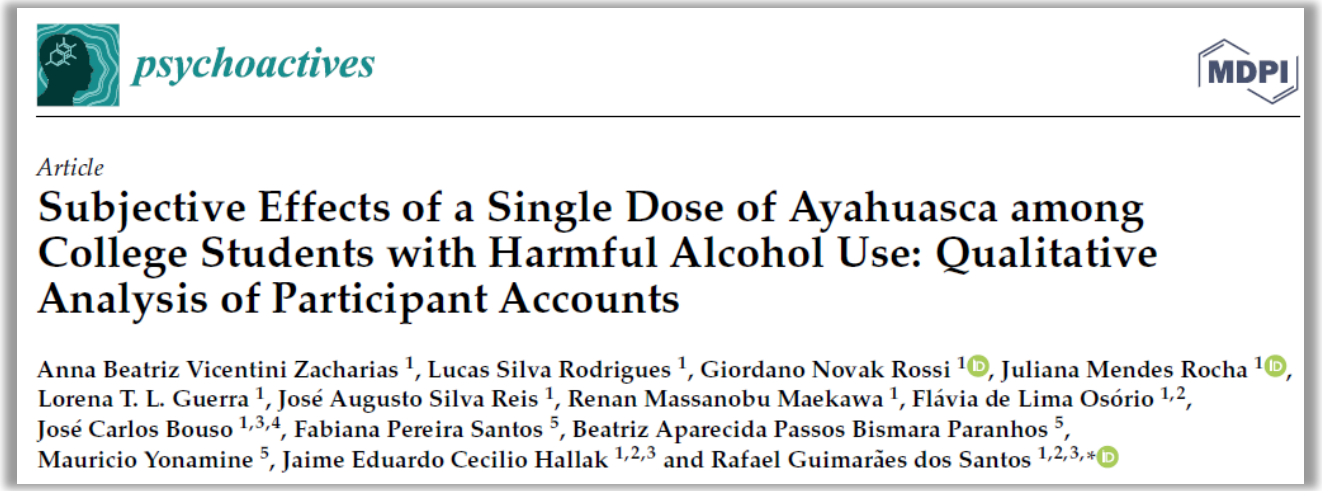
FIGURE 1. Weekly alcohol use before and after the ayahuasca intake (n = 11). *$P < 0.05$, uncorrected. Error bars denote 1 SEM.

Source: Silva et al., 2024.

How does ayahuasca produce its effects?

Psychological mechanisms of action

- Qualitative analysis 21 days after drug intake (n = 6).
- Link between insights and positive emotions and reductions in weekly alcohol use.



psychoactives

MDPI

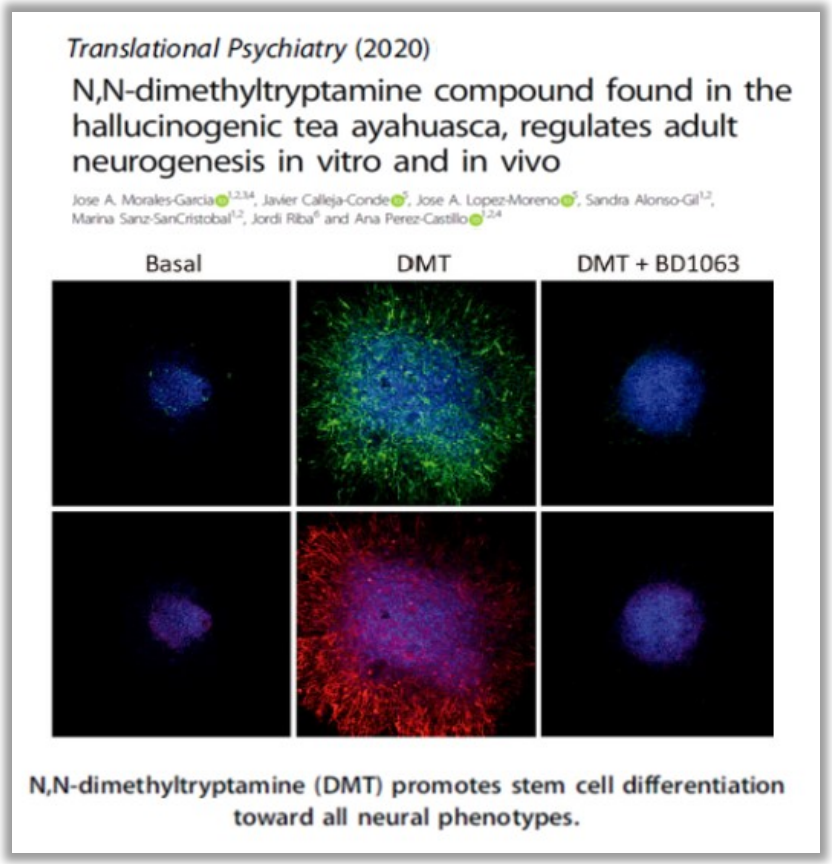
Article

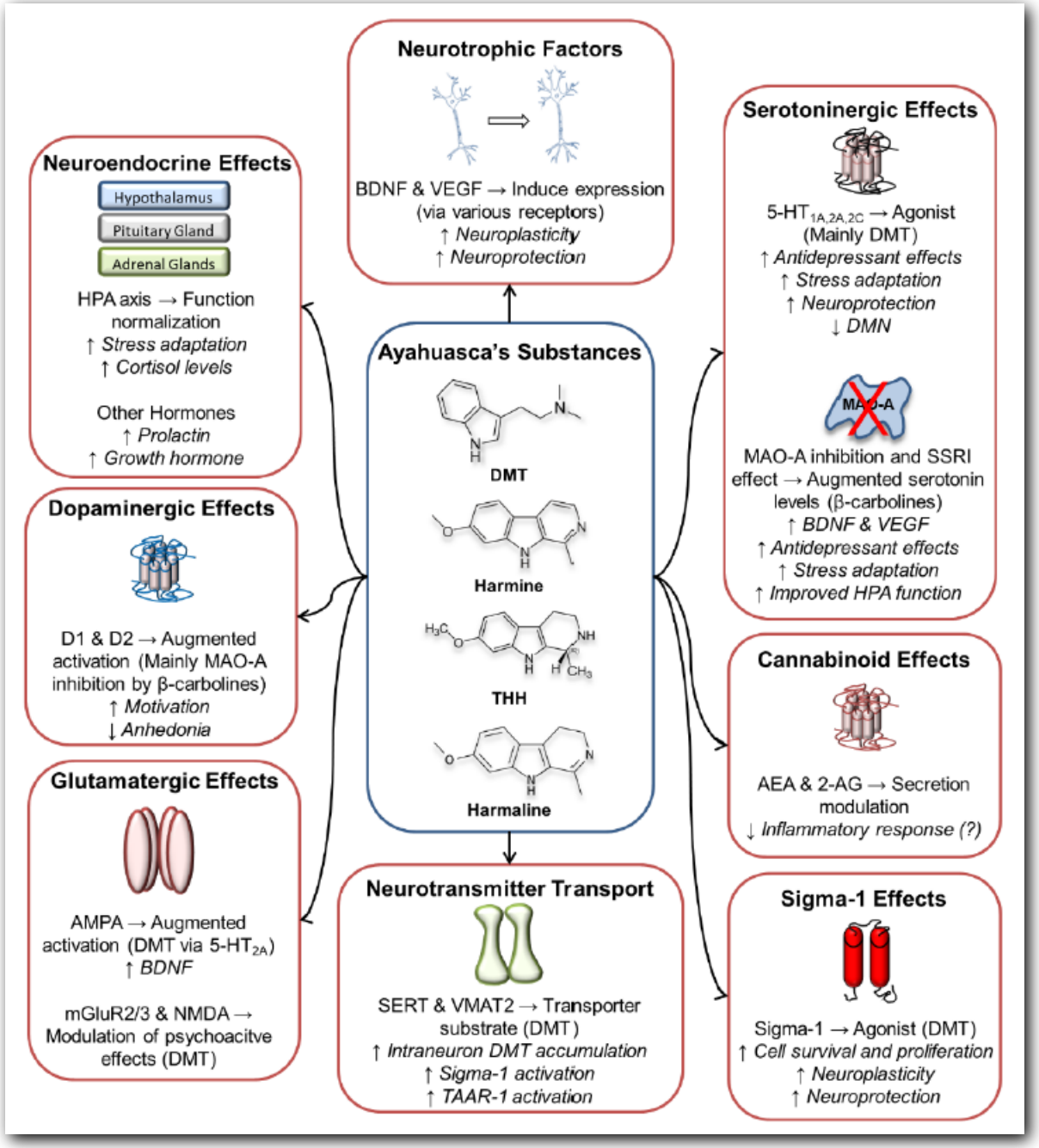
Subjective Effects of a Single Dose of Ayahuasca among College Students with Harmful Alcohol Use: Qualitative Analysis of Participant Accounts

Anna Beatriz Vicentini Zacharias [1], Lucas Silva Rodrigues [1], Giordano Novak Rossi [1], Juliana Mendes Rocha [1], Lorena T. L. Guerra [1], José Augusto Silva Reis [1], Renan Massanobu Maekawa [1], Flávia de Lima Osório [1,2], José Carlos Bouso [1,3,4], Fabiana Pereira Santos [5], Beatriz Aparecida Passos Bismara Paranhos [5], Mauricio Yonamine [5], Jaime Eduardo Cecilio Hallak [1,2,3] and Rafael Guimarães dos Santos [1,2,3,*]

Source: Vientini et al., 2023.

Biological mechanisms of action





Source: Morales-Garcia et al., 2020; Rossi et al., 2022.

What is ibogaine?

Ibogaine and Culture

- Iboga (*Tabernanthe iboga*) is used for ritual and therapeutic purposes.
- It is used by indigenous groups in Congo, Cameroon, and Gabon (national heritage, 2000).
- Ritual use is legal in those countries.

💡 "**Tabernanthe iboga**" de son nom scientifique, l'Iboga est au Gabon ce que la samba est au Brésil, la vodka à la Russie, la pizza à l'Italie...
Décrété « patrimoine national », le "bois sacré" comme l'appelle les puristes, est un arbuste dont la racine, est consommée dans notre pays au cours de rites initiatiques, sous forme de poudre, et ce depuis des siècles.

L'iboga inscrite au patrimoine national

Ainsi en a décidé le récent conseil des ministres qui répond à une préoccupation des peuples utilisateurs, émise lors du dernier séminaire organisé par le laboratoire universitaire de la tradition orale (Luto) sur le Bwiti.

OTEMBE-NGUEMA

LORSQUE l'un des séminaristes, au foyer Avaro de l'UOB où se tenait la réunion sur le Bwété, avait pris l'engagement de transmettre à qui de droit les recommandations et résolutions qui en étaient issues, pour qu'elles ne se noient pas dans les marais de l'oubli, personne n'y avait porté grand intérêt, tant on sait le sort souvent réservé aux conclusions des rencontres de ce genre.

Même si le laboratoire universitaire de la tradition orale (Luto) n'y est pour rien, la décision du Conseil des ministres du mercredi 6 juillet dernier d'inscrire l'iboga au patrimoine national est le signal d'une révolution imminente, celle qui permettra au pays de renouer avec sa véritable identité et de résoudre, on l'espère, les grands problèmes de la philosophie : le rôle de l'homme dans l'univers, la divinité, les valeurs morales, le sens de l'histoire. Des questions que n'occultent ni n'ignorent les cosmogonies gabonaises, ainsi que l'ont souvent prétendu les préjugés.

L'iboga qu'il va falloir protéger au plan international et dont il faut mettre fin à l'exportation illicite, est une plante – petit arbuste des sous-bois – dont les racines sont utilisées lors des cérémonies

L'iboga, une plante mystérieuse, désormais patrimoine national et protégée de l'exploitation illicite. (Ph. Ahmed Minkoh)

rituelles, notamment au cours du bwété, une société initiatique secrète. La consommation de ce puissant psychotrope – on affirme qu'il ne pousse qu'au Gabon – profondément ancré dans les cultures et la vie spirituelle gabonaise, permet de rentrer en communion avec les ancêtres.

Découverte par l'explorateur français Griffon du Bellay, en 1864, la tabernanthe Ibogade, nom scientifique de l'Iboga, a été étudiée dès 1888, par le botaniste français Baillon. Plusieurs autres scientifiques ont ensuite isolé les principes actifs de cette plante, au nombre desquels, le chercheur américain Howard Lotsof qui a déposé un brevet sur une thérapie à base d'Iboga permettant de lutter contre les dépendances aux opiacés tels que l'héroïne.

Selon les explications du Pr Jean-Noël Gassita qui a réalisé de nombreux travaux sur la plante, l'ibogaïne, l'un des alcaloïdes contenus dans l'Iboga, possède des vertus thérapeutiques et a commencé à être utilisé aux États-Unis d'Amérique pour le sevrage des toxicomanes. Ce pays à l'étendue d'un continent a également accueilli, il n'y a pas longtemps, une conférence sur les propriétés de l'Iboga, à laquelle ont pris part le pharmacien gabonais susmentionné et Mme Francine Yveline Nnoh, une tradipraticienne, initiée au mystère de l'Iboga par l'un des grands bwitistes du Gabon, M. Minko-mi-Nzoughe, orginiaire de l'Ogooué-Ivindo, au Nord-Est du pays.

Signalons que l'Iboga est également un tonique neuro-musculaire et un anti-asthénique. Elle agit aussi contre la faim et la soif. Cependant, elle ne présente pas, ainsi qu'on en a fait courir le bruit, des vertus aphrodisiaques, les scientifiques qui l'ont étudié, sont formels là dessus.

l'union

Source: L'Union; www.legigabon.com.

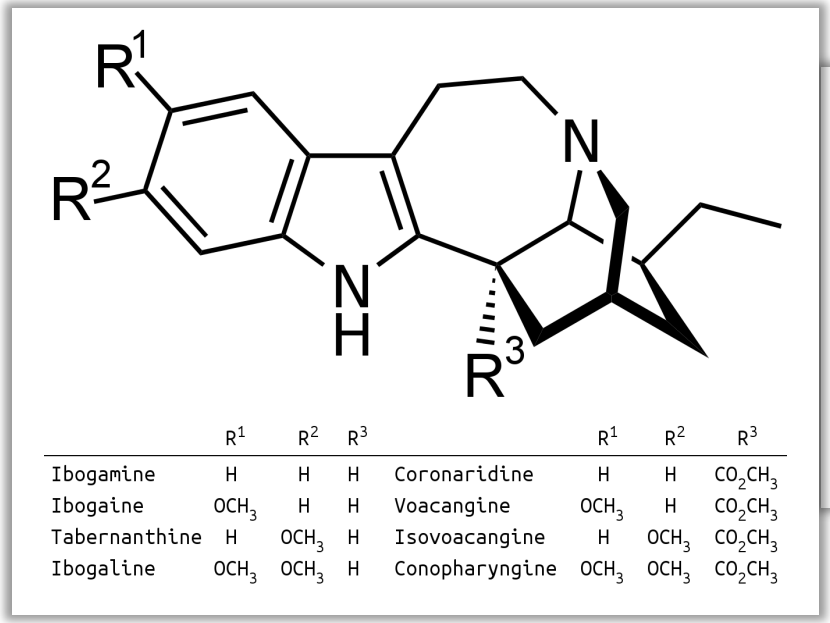
Ibogaine and Botany

- Iboga is prepared with the root bark of the *Tabernanthe iboga* shrub.
- “Bois sacré”: sacred wood.

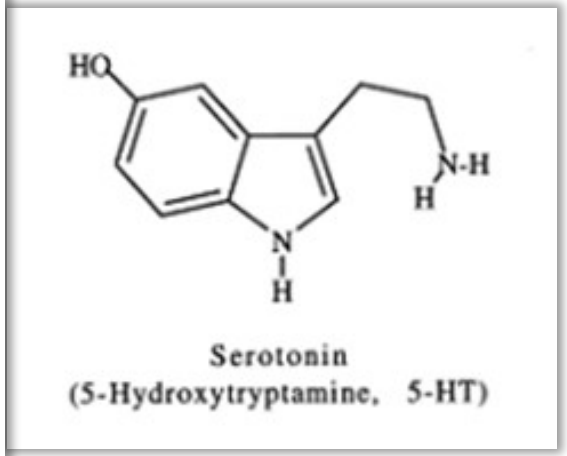
Source: www.legigabon.com.

Ibogaine Alkaloids

- *Tabernanthe iboga* root bark is rich in ibogaine, among other alkaloids (ibogamine, ibogaline, voacangibe).
- These compounds share their chemical structure with serotonin (5-HT).



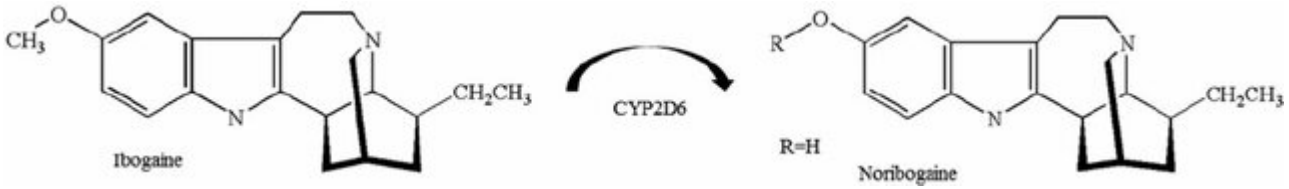
	R^1	R^2	R^3		R^1	R^2	R^3
Ibogamine	H	H	H	Coronaridine	H	H	CO_2CH_3
Ibogaine	OCH_3	H	H	Voacangine	OCH_3	H	CO_2CH_3
Tabernanthine	H	OCH_3	H	Isovoacangine	H	OCH_3	CO_2CH_3
Ibogaline	OCH_3	OCH_3	H	Conopharyngine	OCH_3	OCH_3	CO_2CH_3



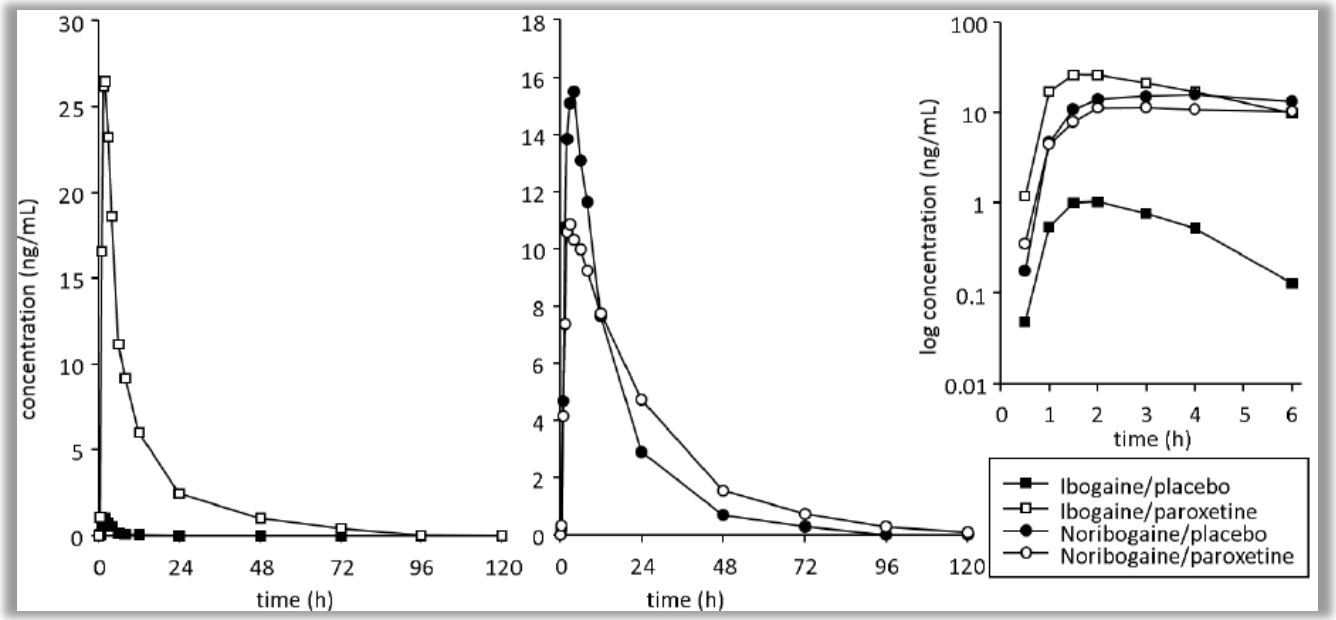
Serotonin
(5-Hydroxytryptamine, 5-HT)

Source: Bading-Taika et al., 2018.

Ibogaine Alkaloids



- The main active metabolite of ibogaine is noribogaine.
- Conversion of ibogaine to noribogaine is mediated primarily by CYP2D6.
- Noribogaine has a longer half-life (13 h vs 2.5-7.5 h).



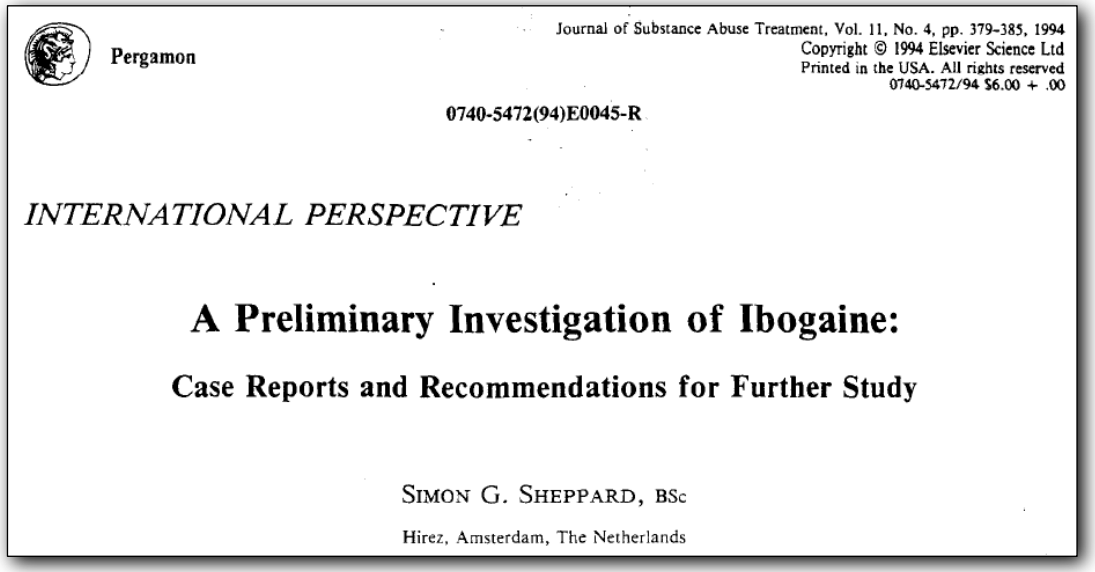
20 mg dose of ibogaine in 21 healthy subjects pretreated for 6 days with placebo or the CYP2D6 inhibitor paroxetine.

Source: Mash et al., 2001; Glue et al. 2015; Litjens & Brunt, 2016.

What are the effects of ibogaine on drug use?

Observational studies / Case series

- Less use of opiates (heroin, methadone), stimulants (cocaine), and alcohol.
- Reduced opiate withdrawal symptoms.
- Usually using single, high doses (7.5-55 mg/kg) of unknown purity in non-controlled settings.



Pergamon

Journal of Substance Abuse Treatment, Vol. 11, No. 4, pp. 379–385, 1994
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0740-5472(94)E0045-R

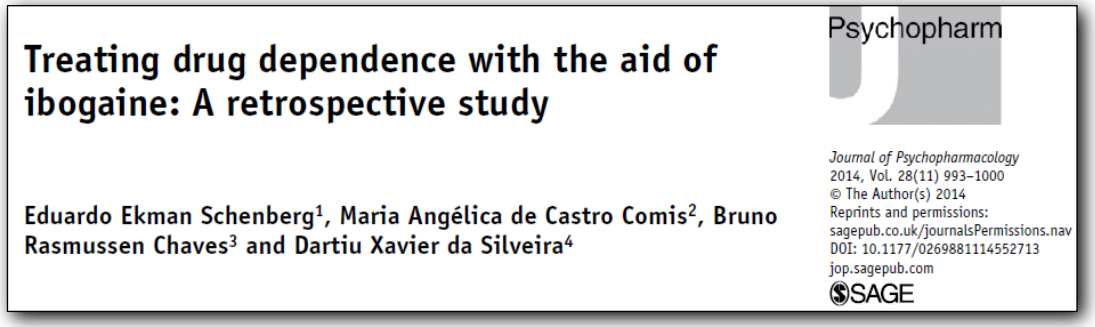
INTERNATIONAL PERSPECTIVE

A Preliminary Investigation of Ibogaine:

Case Reports and Recommendations for Further Study

SIMON G. SHEPPARD, BSc

Hirez, Amsterdam, The Netherlands



Treating drug dependence with the aid of ibogaine: A retrospective study

Eduardo Ekman Schenberg[1], Maria Angélica de Castro Comis[2], Bruno Rasmussen Chaves[3] and Dartiu Xavier da Silveira[4]

Psychopharm

Journal of Psychopharmacology
2014, Vol. 28(11) 993–1000
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DOI: 10.1177/0269881114552713
jop.sagepub.com
SAGE

Source: Sheppard, 1994; Schenberg et al. 2014.

Observational studies / Case series

- Several types of ibogaine products (root bark, alkaloid extracts, ibogaine hydrochloride/HCl).
- Highly variable composition:
  - 0.6-1.2% (iboga root bark)
  - 8.2-32.9% (alkaloid extracts)
  - 61.5-73.4% (ibogaine HCl)
- Unknown substances in several samples.

Table 2. Alkaloid summary

	Iboga Root Bark (n = 6)			TA (n = 5)			Ibogaine HCl (n = 3)		
	N	Ave.	Range	N	Ave.	Range	N	Ave.	Range
Ibogaine	5	6.2%	0.6%-11.2%	5	17.8%	8.2%-32.9%	3	67.0%	61.6%-73.4%
Ibogaline	2	0.8%	0.1%-1.5%	5	0.69%%	0.2%-2.3%	1	7.2%	--
Ibogamine	4	0.98%	0.3%-2.3%	5	4.3%	0.6%-16.4%	3	5.9%	2.1%-8.7%
Voacangine	1	0.2%	--	5	0.25%	0.1%-0.6%	0	--	--
Iboleutine	0	--	--	5	0.27%	0.1%-0.6%	0	--	--

Source: Bouso et al. 2020.

Preclinical studies

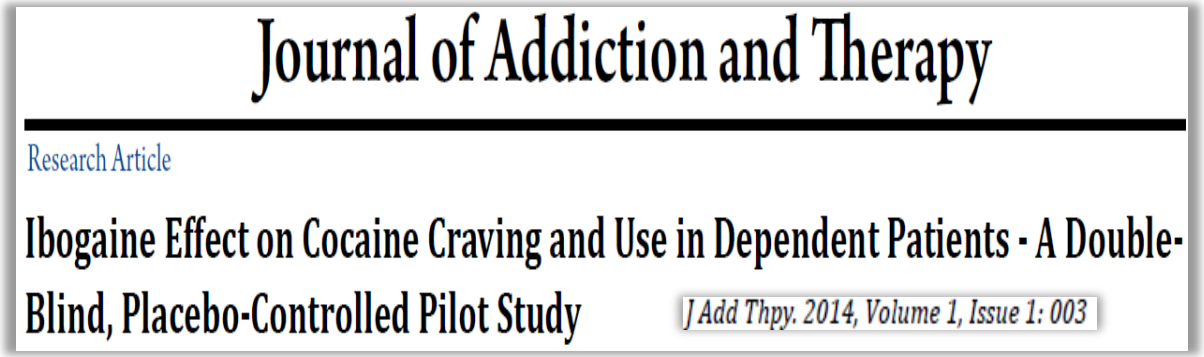
- Reductions in alcohol, morphine, opioids, and amphetamine self-administration (>72h).
- However, reductions in amphetamine- and morphine-induced conditioned place preference were not observed.

Drug self-administration		***Effect of ibogaine***
Overall		↓
Drugs used	Amphetamine	↓
	Opioids	↓
	Alcohol	↓
Moment of measurement after ibogaine dosing	0–24 h	↓↓
	24–72 h	↓
	>72 h	↓
No difference in gender, species or dosing		
Conditioned place preference		***Effect of ibogaine***
Overall		–
Drugs used	Amphetamine	–
	Morphine	–
Moment of measurement after ibogaine dosing	0–24 h	–
	24–72 h	–
No difference in gender, species or dosing		

Source: Belgers et al. 2016.

Clinical studies

- Few open-label studies and a single double-blind trial suggest reductions in opiate (mainly heroin) and stimulant (cocaine) use.
- Reduced opiate withdrawal symptoms and depressive symptoms were also reported.

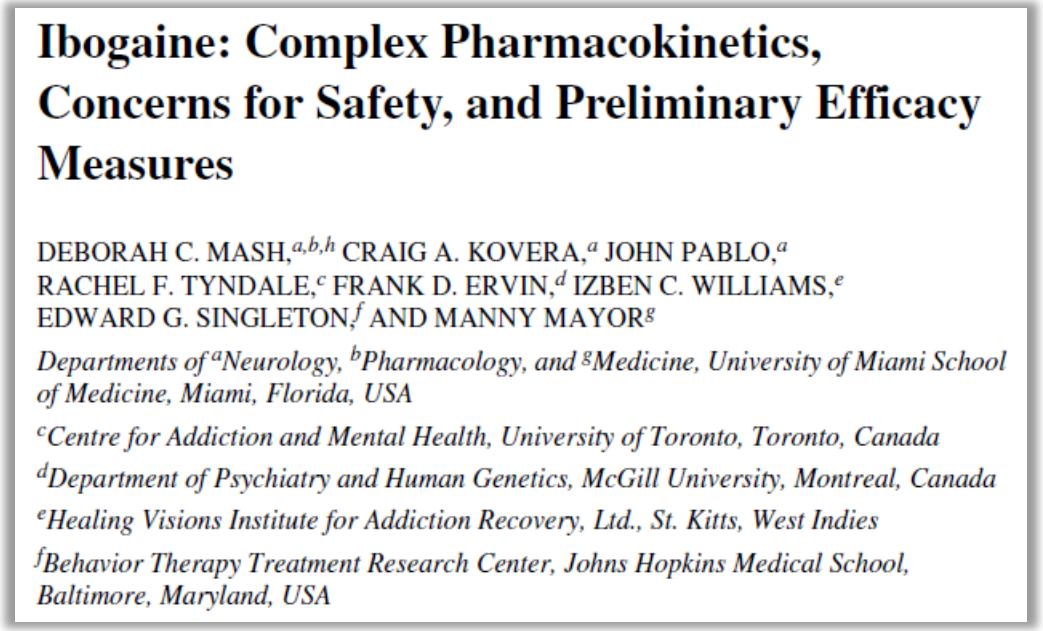


Journal of Addiction and Therapy

Research Article

Ibogaine Effect on Cocaine Craving and Use in Dependent Patients - A Double-Blind, Placebo-Controlled Pilot Study

J Add Thpy. 2014, Volume 1, Issue 1: 003



Ibogaine: Complex Pharmacokinetics, Concerns for Safety, and Preliminary Efficacy Measures

DEBORAH C. MASH,[a,b,h] CRAIG A. KOVERA,[a] JOHN PABLO,[a] RACHEL F. TYNDALE,[c] FRANK D. ERVIN,[d] IZBEN C. WILLIAMS,[e] EDWARD G. SINGLETON,[f] AND MANNY MAYOR[g]

Departments of [a]Neurology, [b]Pharmacology, and [g]Medicine, University of Miami School of Medicine, Miami, Florida, USA

[c]Centre for Addiction and Mental Health, University of Toronto, Toronto, Canada

[d]Department of Psychiatry and Human Genetics, McGill University, Montreal, Canada

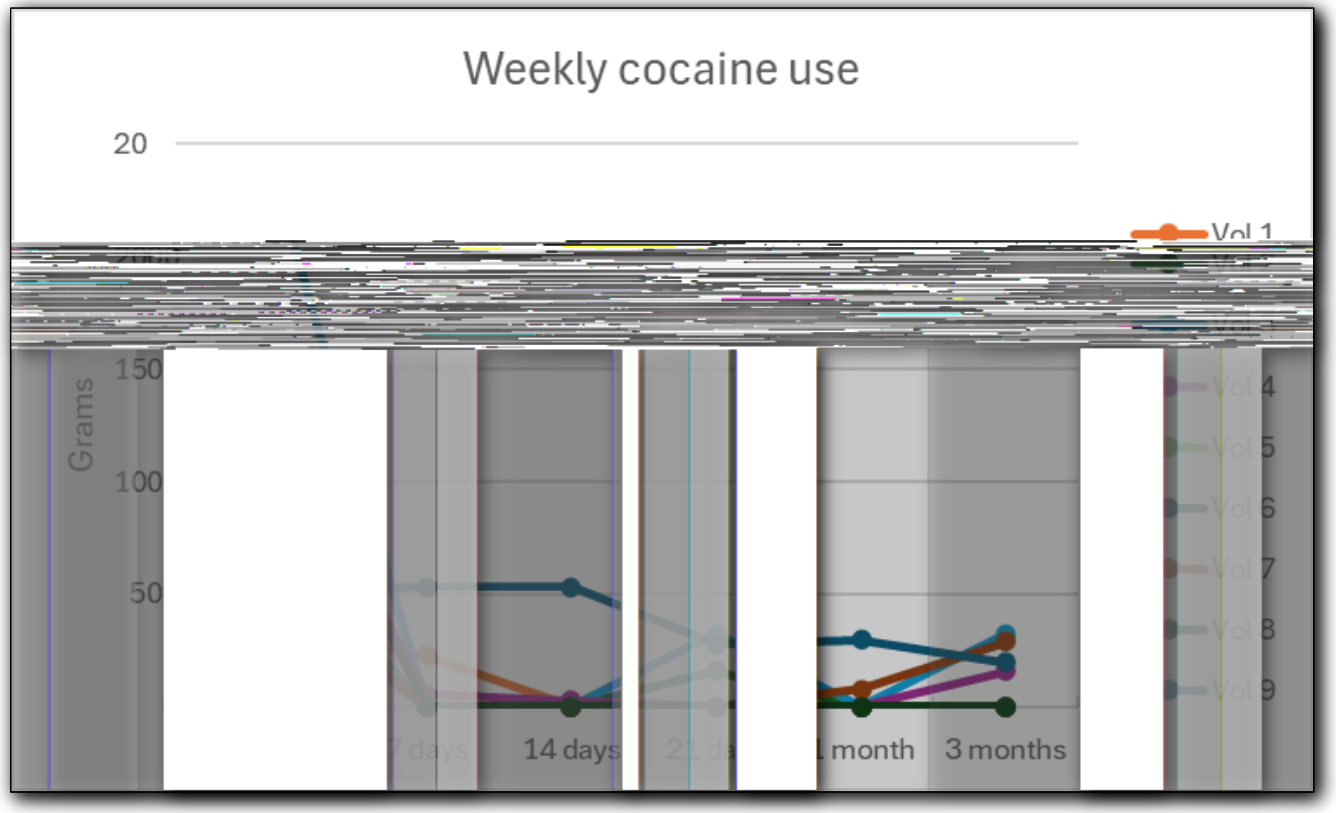
[e]Healing Visions Institute for Addiction Recovery, Ltd., St. Kitts, West Indies

[f]Behavior Therapy Treatment Research Center, Johns Hopkins Medical School, Baltimore, Maryland, USA

Source: Prior & Prior, 2014; Mash et al., 2000.

Clinical studies

- Single doses of ibogaine (20-400mg) in adults with moderate/severe alcohol and cocaine use disorders.
- Single-blind (n = 9).
- Reductions in weekly alcohol and cocaine use.



Source: Rocha et al. 2025.

Clinical studies

- Ibogaine was well tolerated:
  - Sedation (53%)
  - Nausea (36%)
  - Anxiety (33%)
  - Difficulty in concentration (30%)
- No serious adverse effects.
- Transient increases in QTc interval (4-12h), with some increases above normative values.

QT INTERVAL

SESSION 1

Patient/Sex/Dose (mg)	Time (h)/QT Interval (ms)							
	0	1	2	3	4	5	6	12
1/H/20	423	448	398	339	398	398	413	436
2/H/80	341	392	366	366	383	426	392	375
3/H/**240**	413	436	388	398	456	435	**470**	**492**
4/**M**/400	391	391	431	452	462	452	418	396
5/**M**/**400**	413	380	420	413	460	426	412	**496**
6/H/**400**	360	378	325	320	372	452	405	378
7/**M**/400	395	387	391	385	424	402	410	424
8/H/400	395	387	391	385	424	402	410	405
9/H/**400**	409	402	395	423	463	**470**	430	423

SESSION 2

Patient/Sex/Dose (mg)	Time (h)/QT Interval (ms)							
	0	1	2	3	4	5	6	12
1/H/40	375	382	335	323	398	398	376	365
2/H/160	366	410	375	426	392	410	392	426
3/H/**320**	363	369	391	431	431	456	447	402

SESSION 3

Patient/Sex/Dose (mg)	Time (h)/QT Interval (ms)							
	0	1	2	3	4	5	6	12
1/H/80	375	392	383	366	412	392	416	376
2/H/240	396	415	418	404	423	412	420	411

Normative value: H=450ms/M=470ms (Framingham)

Source: Rocha et al. 2025.

Clinical studies

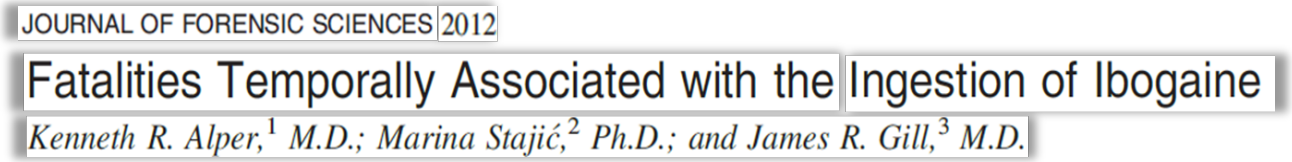
- 25-year-old woman.
- No clinical comorbidities.
- ECG screening/baseline: normal.
- ECG 4-5h: Possible myocardial ischemia / electrolyte imbalance.
- Stable vital signs.
- Asymptomatic (precordial pain, dizziness, dyspnea).
- Coronary Computed Tomography Angiography (CCTA): normal.

Time (hours)	QT Interval (ms)	ECG
1	395	Normal
2	398	Normal
3	391	Normal
4	385	T wave inversion (V1-V3)
5	424	T wave inversion (V1-V3) Minimal ST-segment deviation (V1-V4)
6	402	Normal
12	410	Normal
24	405	Normal

Source: Rocha et al. 2025.

Observational studies / Case series

- 22 fatalities temporally associated with ibogaine (1.5-76h) (1990-2015).
- Several cases of non-fatal QT interval alterations.
- Preexisting medical comorbidities (mainly cardiac) and use of one or more drugs in several cases.
- High doses of uncertain purity, uncontrolled settings with no medical/cardiac support.


JOURNAL OF FORENSIC SCIENCES 2012

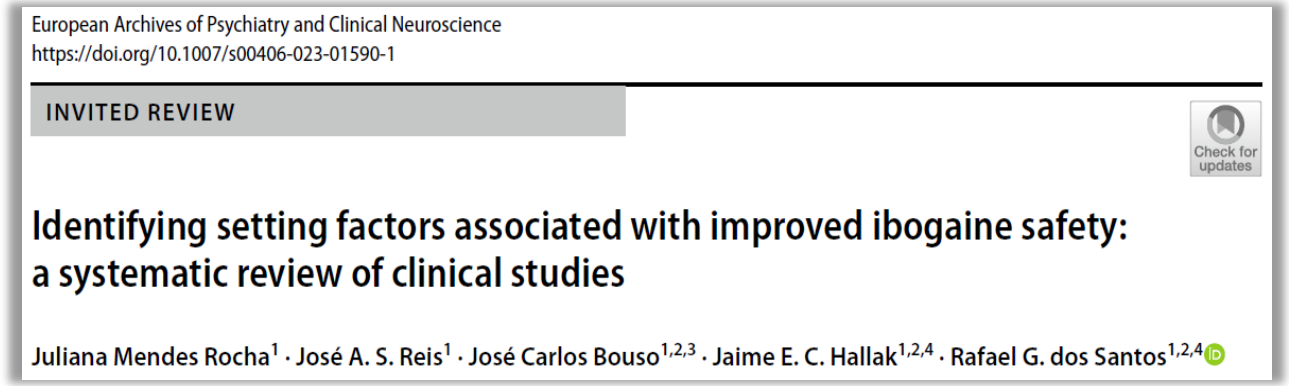
Fatalities Temporally Associated with the Ingestion of Ibogaine

Kenneth R. Alper,[1] M.D.; Marina Stajić,[2] Ph.D.; and James R. Gill,[3] M.D.


Molecules **2015**

The Anti-Addiction Drug Ibogaine and the Heart: A Delicate Relation

Xaver Koenig * and Karlheinz Hilber *


European Archives of Psychiatry and Clinical Neuroscience
https://doi.org/10.1007/s00406-023-01590-1

INVITED REVIEW

Check for updates

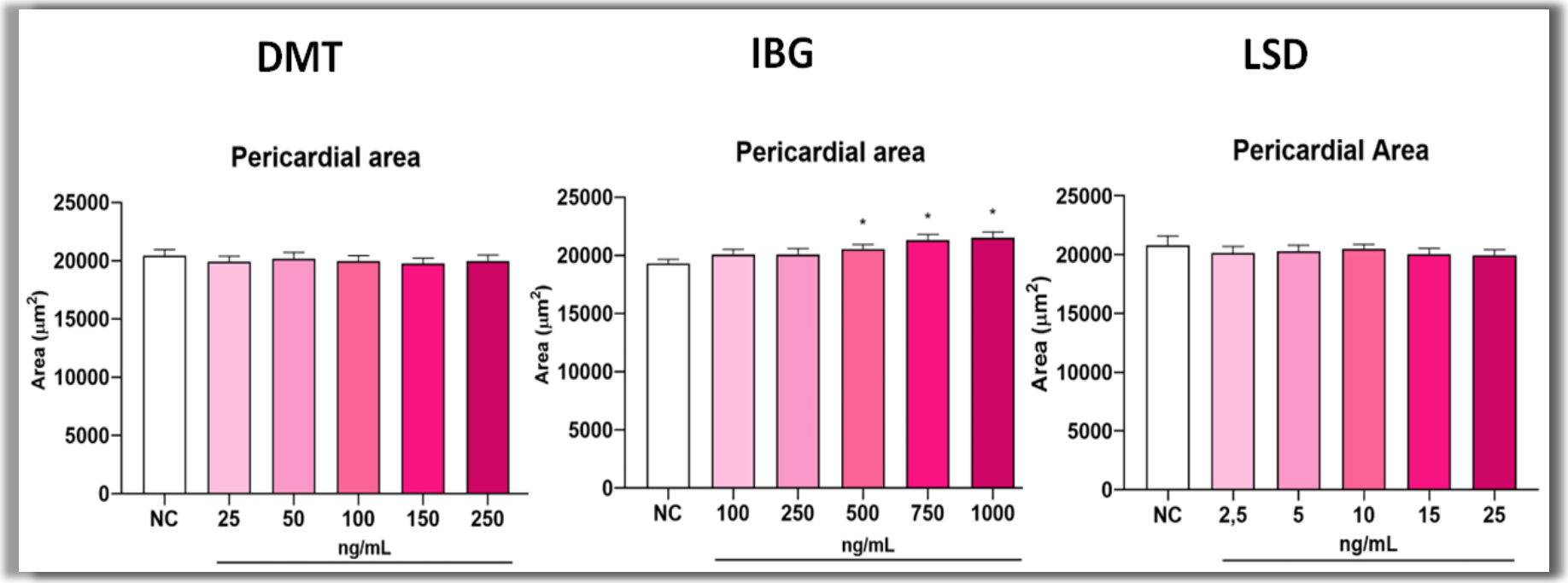
Identifying setting factors associated with improved ibogaine safety: a systematic review of clinical studies

Juliana Mendes Rocha[1] · José A. S. Reis[1] · José Carlos Bouso[1,2,3] · Jaime E. C. Hallak[1,2,4] · Rafael G. dos Santos[1,2,4]

Source: Alpern et al., 2012; Koenig & Hilber, 2015; Rocha et al., 2023.

Preclinical studies

- Zebrafish (*Danio rerio*):
  - LSD: 2,5-25 ng/mL
  - DMT: 25-250 ng/mL
  - Ibogaine: 100-1000 ng/mL



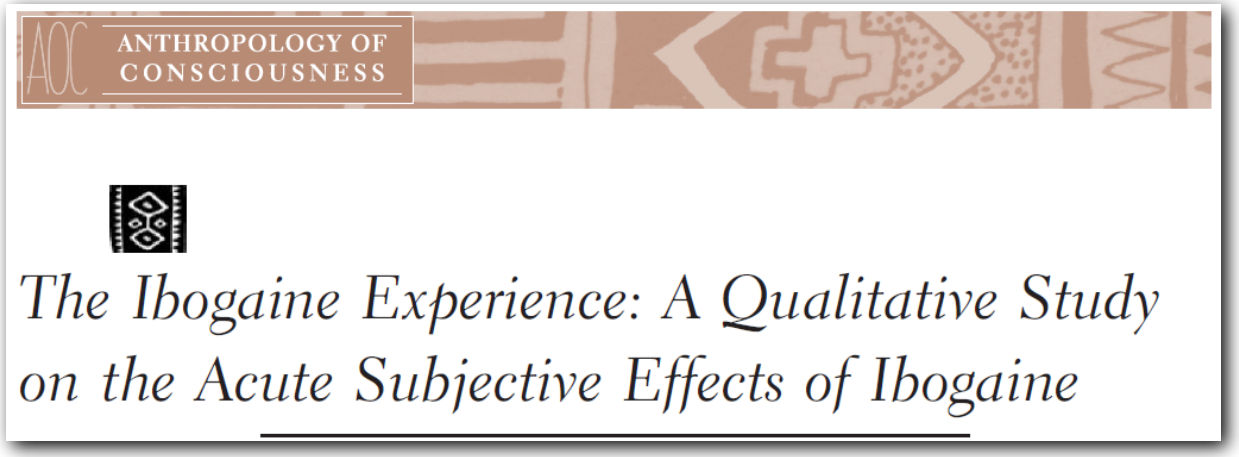
Source: Oliveira et al. 2025.

How does ibogaine produce its effects?

Psychological mechanisms of action

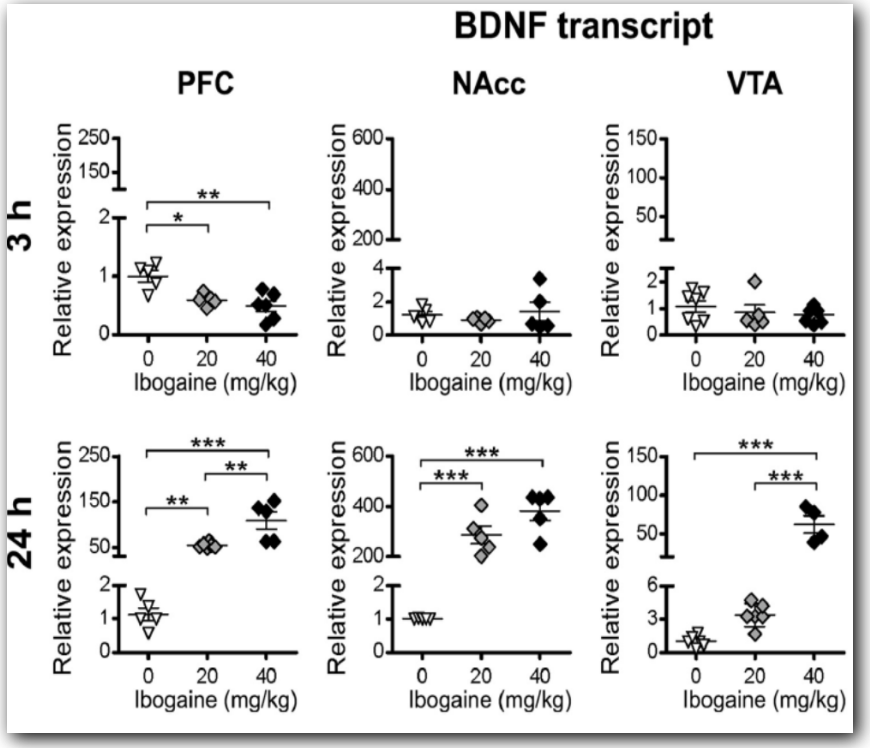
Subjective experiences

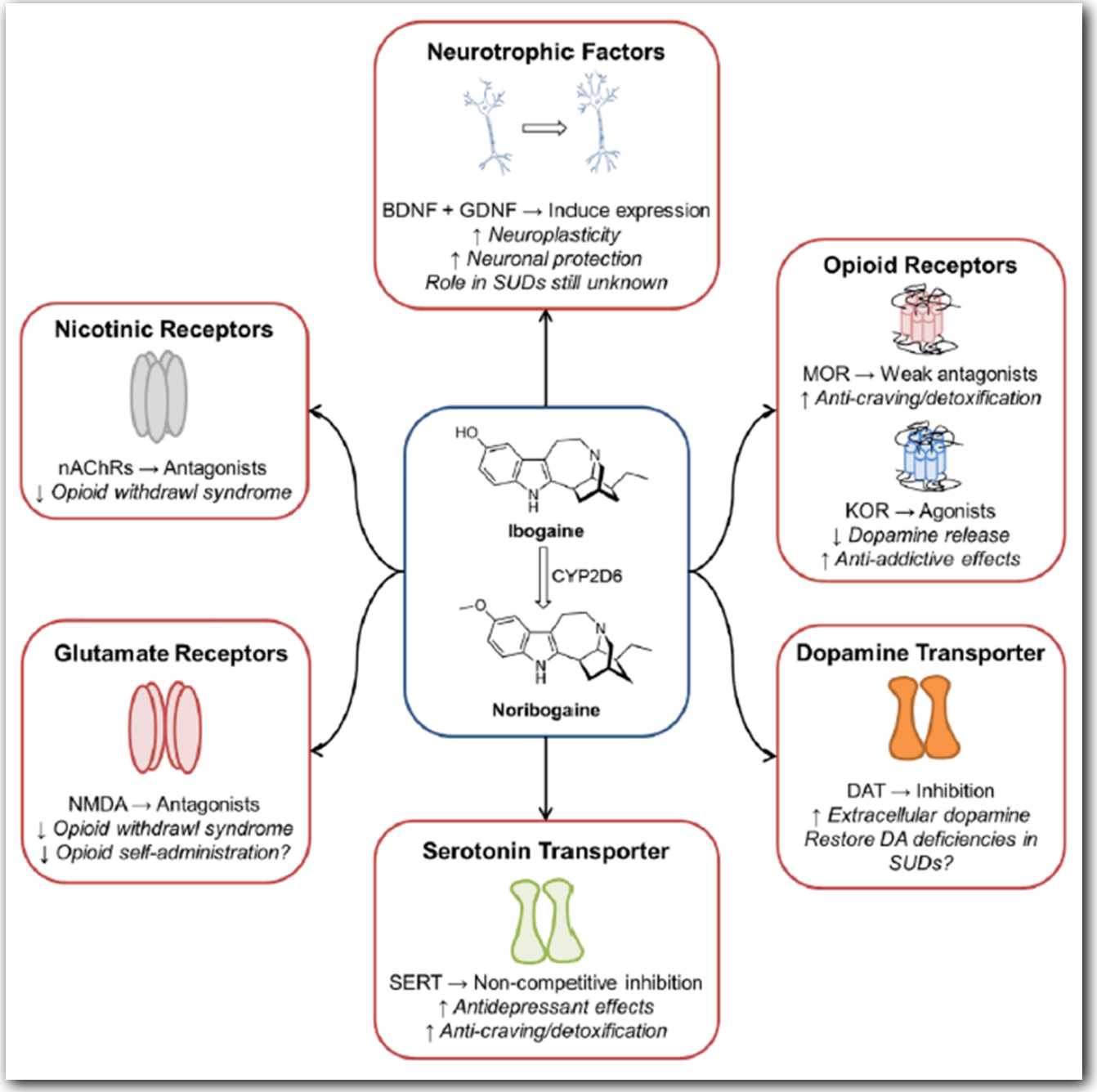
- Self-psychoanalysis;
- Autobiographical memories;
- Empathy and love;
- Prosocial behavior;
- Ego dissolution;
- Spiritual states and transpersonal experiences.



Source: Kohek et al. 2020; Rodríguez-Cano et al., 2022.

Biological mechanisms of action





Source: Marton et al., 2019; Ona et al. 2023.

19e Congrès International d'Addictologie de l'ALBATROS

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