A History of the Science, Politics and Advocacy of ibogaine: A Brief Overview

Howard S. Lotsof
Dora Weiner Foundation
Staten Island, NY

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Ibogaine Found in a West African plant Tabernanthe iboga
Iboga alkaloids are concentrated in the bark of the root
Usable forms include scraped or ground root bark
Total Alkaloid extract

Courtesy Sara Glatt
Proposed as an approved regulated drug
Physical Characteristics of ibogaine

Source Merck Index

Chemical formula \( \text{C}_{20}\text{H}_{26}\text{N}_{2}\text{O} \)
Mol. Wt. 310.42
Melting Point 152-153°
Practically insoluble in water.
Soluble in ethanol, ether, chloroform

Molecular structure
Background: Ibogaine

- Botanical source Tabernanthe iboga. Used for 100s of years in African medicine and religion
- 1901 ibogaine isolated by Dybowski and Landrin
- 1958 molecular structure determined Bartlett et al.
- 1962 Lotsof discovers Antiaddictive effects
- 1991 National Institute on Drug Abuse (NIDA) initiates evaluation of ibogaine
- 1993 Food and Drug Administration (FDA) approves clinical study of ibogaine
- 1995 NIDA Ibogaine Clinical Review Meeting.
Ibogaine Patents


Regulatory and Scientific Development

The first attempt at drug development of ibogaine was by the Dora Weiner Foundation in 1983.

In 1986, a for-profit corporation, NDA International, Inc. was established and subsequently raised 4 million towards the approval of ibogaine, initiating research and patent development.

1991, National Institute on Drug Abuse ibogaine research project.

1993, FDA approval for University of Miami clinical study. Under contract to NDA International, Inc.
Lotsof period historical development
NIDA Initially Rejects Ibogaine Research.

NIDA was petitioned to perform ibogaine research between 1984 - 1990, first by the Dora Weiner Foundation and from 1986 on by NDA International, Inc., a company established to make ibogaine available as an approved medication. In 1991, NIDA formed its Medications Development Division (MDD) and accepted a Product Profile Review (PPR) from NDA International that resulted in NIDA starting their ibogaine research program.
First scientific publication of ibogaine antiaddictive effects - Dzoljic et al. -

**Effect of ibogaine on naloxone-precipitated withdrawal syndrome in chronic morphine-dependent rats.**

Dzoljic ED, Kaplan CD, Dzoljic MR.

Department of Pharmacology, Medical Faculty, Erasmus University, Rotterdam, The Netherlands.

Ibogaine, an indole alkaloid, administered intracerebroventricularly 4-16 micrograms, attenuated a naloxone-precipitated withdrawal syndrome in chronic morphine-dependent rats. It appears that ibogaine has a more consistent effect on certain selective withdrawal signs related to the locomotion. This might explain an attenuating effect of ibogaine on some withdrawal signs. However, due to complex interaction of ibogaine with serotonin and other neurotransmitter systems, the mechanism of ibogaine anti-withdrawal effect remains unknown and requires further elucidation.

PMID: 3233054 [PubMed - indexed for MEDLINE]
National Institute on Drug Abuse (NIDA) funds 85% of drug addiction research worldwide.
NIDA Response to Dzoljic: It doesn’t work


**Ibogaine fails to reduce naloxone-precipitated withdrawal in the morphine-dependent rat.**

*Sharpe LG, Jaffe JH.*

Addiction Research Center, National Institute on Drug Abuse, Baltimore, MD 21224.

Because of anecdotal reports in which ibogaine eliminates opioid withdrawal symptoms in humans, we studied this phenomenon in the rat model. Ibogaine (5, 10, 20 and 40 mg kg⁻¹, s.c.) was administered 15 min before naloxone (0.5 mg kg⁻¹, s.c.) in morphine dependent rats (3 days after the s.c. implantation of a 75 mg morphine pellet). Of the 12 withdrawal signs scored, the only significant changes observed after ibogaine (compared with vehicle control) was a decrease in grooming (10 mg kg⁻¹) and an increase in teeth chatter (5 mg kg⁻¹). In spite of ibogaine’s apparent interaction with several neurotransmitter receptor systems, it does not alleviate opioid withdrawal in this animal model at non-tremorgenic (5 and 10 mg kg⁻¹) or tremorgenic (20 and 40 mg kg⁻¹) doses.

PMID: 2129850 [PubMed - indexed for MEDLINE]
Additional research supports Dr. Dzoljic’s findings. Dr. Stanley D. Glick at Albany Medical College begins the publication of what will become dozens of research papers.

Effects and aftereffects of ibogaine on morphine self-administration in rats.

Glick SD, Rossman K, Steindorf S, Maisonneuve IM, Carlson JN.

Department of Pharmacology and Toxicology (A-136), Albany Medical College, NY 12208.

Ibogaine, a naturally occurring alkaloid, has been claimed to be effective in treating addiction to opiate and stimulant drugs. As a preclinical test of this claim, the present study sought to determine if ibogaine would reduce the intravenous self-administration of morphine in rats. Ibogaine dose dependently (2.5-80 mg/kg) decreased morphine intake in the hour after ibogaine treatment (acute effect) and, to a lesser extent, a day later (aftereffect); while the acute effect could be attributed to abnormal motor behavior (whole body tremors), the aftereffect occurred at a time when ibogaine should have been entirely eliminated from the body and when there was no obvious indication of ibogaine exposure. In some rats, there was a persistent decrease in morphine intake for several days or weeks after a single injection of ibogaine; other rats began to show such persistent changes only after two or three weekly injections whereas a few rats were apparently resistant to prolonged aftereffects. Aftereffects could not be attributed to a conditioned aversion. Although ibogaine also depressed responding acutely in rats trained to bar-press for water, there was no evidence of any aftereffect a day or more later; the interaction between ibogaine and morphine reinforcement was therefore somewhat specific. Further studies are needed to characterize the nature of the ibogaine-morphine interaction as well as to determine if ibogaine also affects the self-administration of other drugs.

PMID: 1868880 [PubMed - indexed for MEDLINE]
Ibogaine effects on cocaine


Inhibitory effects of ibogaine on cocaine self-administration in rats.

Cappendijk SL, Dzoljic MR.

Department of Pharmacology, Faculty of Medicine and Health Sciences, Erasmus University Rotterdam, Netherlands

In order to determine the potential anti-addictive properties of ibogaine, we used the cocaine self-administration model in rats. The results indicate that a single injection of ibogaine (40 mg/kg i.p.) produced a significant decrease of cocaine intake, which remained unaltered for more than 48 h. Since the half-life time of ibogaine is short, this might suggest the involvement of one or several active metabolites of ibogaine in cocaine intake. Repetitive administration of ibogaine on three consecutive days also induced a pronounced decrease of cocaine intake. However, a more prominent inhibitory effect on cocaine intake was observed in animals treated repeatedly with ibogaine (40 mg/kg i.p.), once each week for 3 consecutive weeks. These results indicate that ibogaine or its metabolite(s) is a long-lasting interruptor of cocaine dependence, which supports similar observations from uncontrolled clinical studies.

PMID: 8243561 [PubMed - indexed for MEDLINE]
Ibogaine effects on cocaine
(Cappendijk & Dzoljic)

Fig. 1. Effect of a single dose of ibogaine (10–40 mg/kg i.p., n = 3–7 per dose) on cocaine intake in rats. The baseline cocaine intake (■)
Attenuation of alcohol intake by ibogaine in three strains of alcohol-preferring rats.

Rezvani AH, Overstreet DH, Lee YW.

Skipper Bowles Center for Alcohol Studies, University of North Carolina School of Medicine at Chapel Hill, USA.

Alcohol-preferring (P), Fawn-Hooded (FH) and alcohol-accepting (AA) rats were injected intraperitoneally (IP) or subcutaneously (SC) with different doses (10, 30, and 60 mg/kg) of ibogaine or vehicle. In a separate experiment, FH rats were administered intragastrically (IG) with either 60 mg/kg of ibogaine or vehicle for 5 days. In addition, the effects of ibogaine on blood alcohol concentrations were measured. Our data show that, contrary to the SC administration of ibogaine, IP administration of the agent significantly and dose-dependently reduced alcohol intake in these rats. Subchronic IG administration of 60 mg/kg of ibogaine into FH rats significantly reduced alcohol intake without the development of tolerance or a significant effect on food or water intake. A single IP injection of 60 mg/kg ibogaine into FH rats did not affect the blood alcohol levels. These results show that ibogaine when injected IP or IG, but not SC, can significantly reduce alcohol intake without an effect on blood alcohol concentrations or food intake. These findings may suggest the involvement of ibogaine's metabolite(s) in reducing alcohol intake. Although the neuronal mechanism(s) of action of ibogaine on the regulation of alcohol intake is not fully understood, it is speculated that ibogaine or its metabolite(s) exerts its attenuating effect on alcohol intake by modulating neurotransmitters/neuromodulators proposed to be involved in regulation of alcohol consumption.

PMID: 8545483 [PubMed - indexed for MEDLINE]
Ibogaine effects on alcohol
(Rezvani et al. 1995)

FIG. 1. Effects of different doses of Ibogaine (Ibog) and control vehicle on alcohol intake in FH, AA, and P rats. Data are means ± SEM. *p < 0.05, **p < 0.002, and ***p < 0.001 compared with the corresponding control vehicle.
Opioid withdrawal in human subjects


Treatment of acute opioid withdrawal with ibogaine.

Alper KR, Lotsof HS, Frenken GM, Luciano DJ, Bastiaans I.

Department of Psychiatry, New York University School of Medicine, NY 10016, USA. kra1@is9.nyu.edu

Ibogaine is an alkaloid with putative effect in acute opioid withdrawal. Thirty-three cases of treatments for the indication of opioid detoxification performed in non-medical settings under open label conditions are summarized involving an average daily use of heroin of 64 +/- 50 grams, primarily by the intravenous route. Resolution of the signs of opioid withdrawal without further drug seeking behavior was observed within 24 hours in 25 patients and was sustained throughout the 72-hour period of posttreatment observation. Other outcomes included drug seeking behavior without withdrawal signs (4 patients), drug abstinence with attenuated withdrawal signs (2 patients), drug seeking behavior with continued withdrawal signs (1 patient), and one fatality possibly involving surreptitious heroin use. The reported effectiveness of ibogaine in this series suggests the need for systematic investigation in a conventional clinical research setting.

Publication Types:

- Clinical Trial

PMID: 10506904 [PubMed - indexed for MEDLINE]
Ibogaine in the treatment of heroin withdrawal.

Mash DC, Kovera CA, Pablo J, Tyndale R, Ervin FR, Kamlet JD, Hearn WL.

PMID: 11705106 [PubMed - indexed for MEDLINE]
Return to preaddictive state?

Ibogaine effects on sweet preference and amphetamine induced locomotion: Implications for drug addiction.

Blackburn JR, Szumlinski KK.

Department of Psychology, McMaster University, Hamilton, Ontario, Canada. jrblackb@ilos2.dal.ca

The neural basis of ibogaine's effects on drug-related behaviours is unclear. One possibility is that ibogaine interferes with the shared capacity of many addictive agents to stimulate brain dopamine activity, but reports of ibogaine effects on dopamine activity have been inconsistent. Our study suggests such inconsistencies may result from variations in prior drug exposure. If ibogaine blocks dopamine activity, then it should, like dopamine blockers, decrease preference for natural rewards such as sweet solutions. However, 40 mg/kg ibogaine i.p. did not decrease preference for a glucose + saccharin solution when it was administered to male Long Evans rats 24 h prior to test in Experiment 1. Nor did ibogaine attenuate conditioned preference for a neutral flavour previously paired with sweet taste in Experiment 2. In Experiment 3, effects of 40 mg/kg ibogaine on amphetamine-induced locomotion were investigated in drug-naïve and drug-experienced (four prior doses of 1.5 mg/kg amphetamine) rats. Locomotion was significantly lower in those ibogaine-treated rats that had previously been exposed to amphetamine than in those that had not. Thus, ibogaine may serve to decrease induced levels of dopamine activity in drug-experienced animals or humans from elevated, sensitized levels back to baseline levels. This could lead to a reduction of sensitized levels of drug craving in addiction.

PMID: 9475818 [PubMed - indexed for MEDLINE]
Tissue distribution and availability


**Tissue distribution of ibogaine after intraperitoneal and subcutaneous administration.**

**Hough LB, Pearl SM, Glick SD.**

Department of Pharmacology and Neuroscience, Albany Medical College, NY 12208, USA.

The distribution of the putative anti-addictive substance ibogaine was measured in plasma, brain, kidney, liver and fat after ip and sc administration in rats. One hr after ip dosing (40 mg/kg), drug levels ranged from 106 ng/ml (plasma) to 11,308 ng/g (fat), with significantly higher values after sc administration of the same dose. Drug levels were 10-20 fold lower 12 hr after the same dose. These results suggest that: 1) ibogaine is subject to a substantial "first pass" effect after ip dosing, demonstrated by higher drug levels following the sc route, 2) ibogaine shows a large accumulation in adipose tissue, consistent with its lipophilic nature, and 3) persistence of the drug in fat may contribute to a long duration of action.

PMID: 8632705 [PubMed - indexed for MEDLINE]
NIDA contracts neurotoxicologist Mark Molliver to determine ibogaine neurotoxicity

Ibogaine induces glial activation in parasagittal zones of the cerebellum.

O'Hearn E, Long DB, Molliver ME.

Department of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD 21205.

Ibogaine, an indole alkaloid, has been proposed for treatment of drug addiction, yet its mechanism, site of action, and possible neurotoxicity have not been determined. Since neuronal injury is known to activate neuroglial cells, we investigated potential neurotoxic effects of this drug in rats by examining expression of specific glial markers. After treatment with ibogaine (100 mg kg-1 i.p.; 1-3 doses), we observed increased cytochemical markers in both microglia (OX-6, OX-42, W3/25) and astrocytes (GFAP), associated with striking morphologic changes in these cells. Activated glial cells were restricted to longitudinally oriented, parasagittal stripes within the vermis of cerebellar cortex. The ibogaine-induced activation of cerebellar glial cells is highly suggestive of neuronal degeneration, most likely of Purkinje cells.

PMID: 8477052 [PubMed - indexed for MEDLINE]
Ibogaine researcher Helen Molinari responded


Ibogaine neurotoxicity: a re-evaluation.

Molinari HH, Maisonneuve IM, Glick SD.

Department of Pharmacology and Neuroscience, Albany Medical College, NY 12208, USA.

Ibogaine is claimed to be an effective treatment for opiate and stimulant addiction. O'Hearn and Molliver, however, showed that ibogaine causes degeneration of cerebellar Purkinje cells in rats. The present study re-examined cerebellar responses to the high doses of ibogaine used by O'Hearn and Molliver (100 mg/kg or 3 x 100 mg/kg) and sought to determine whether a lower dose (40 mg/kg), one effective in reducing morphine and cocaine self-administration, produced similar responses. Purkinje cell degeneration was evaluated with a Fink-Heimer II stain, and enhanced glial cell activity with an antibody to glial fibrillary acidic protein. Every rat treated with the high dose of ibogaine displayed clear evidence of Purkinje cell degeneration. The degeneration consistently occurred in the intermediate and lateral cerebellum, as well as the vermis. Purkinje cells in lobules 5 and 6 were particularly susceptible. Given the response properties of cells in these lobules, this finding suggests any long-term motor deficit produced by ibogaine-induced degeneration should preferentially affect the head and upper extremity. In marked contrast, rats given the smaller dose of ibogaine displayed no degeneration above the level seen in saline-treated animals. When combined with information on other compounds, these data suggest that the degenerative and 'anti-addictive' properties of ibogaine reflect different actions of the drug.

PMID: 8930373 [PubMed - indexed for MEDLINE]
The olivocerebellar projection mediates ibogaine-induced degeneration of Purkinje cells: a model of indirect, trans-synaptic excitotoxicity.

O’Hearn E, Molliver ME.

Department of Neuroscience, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205, USA.

Ibogaine, an indole alkaloid that causes hallucinations, tremor, and ataxia, produces cerebellar neurotoxicity in rats, manifested by degeneration of Purkinje cells aligned in narrow parasagittal bands that are coextensive with activated glial cells. Harmaline, a closely related alkaloid that excites inferior olivary neurons, causes the same pattern of Purkinje cell degeneration, providing a clue to the mechanism of toxicity. We have proposed that ibogaine, like harmaline, excites neurons in the inferior olive, leading to sustained release of glutamate at climbing fiber synapses on Purkinje cells. The objective of this study was to test the hypothesis that increased climbing fiber activity induced by ibogaine mediates excitotoxic Purkinje cell degeneration. The inferior olive was pharmacologically ablated in rats by a neurotoxic drug regimen using 3-acetylpyridine, and cerebellar damage attributed to subsequent administration of ibogaine was analyzed using immunocytochemical markers for neurons and glial cells. The results show that ibogaine administered after inferior olive ablation produced little or no Purkinje cell degeneration or glial activation. That a lesion of the inferior olive almost completely prevents the neurotoxicity demonstrates that ibogaine is not directly toxic to Purkinje cells, but that the toxicity is indirect and dependent on integrity of the olivocerebellar projection. We postulate that ibogaine-induced activation of inferior olivary neurons leads to release of glutamate simultaneously at hundreds of climbing fiber terminals distributed widely over the surface of each Purkinje cell. The unique circuitry of the olivocerebellar projection provides this system with maximum synaptic security, a feature that confers on Purkinje cells a high degree of vulnerability to excitotoxic injury.

PMID: 9348351 [PubMed - indexed for MEDLINE]
Xu et al. eventually produce research showing no neurotoxicity at clinical doses (2000)

A dose-response study of ibogaine-induced neuropathology in the rat cerebellum.

Xu Z, Chang LW, Slikker W Jr, Ali SF, Rountree RL, Scallet AC.

Department of Pathology, University of Arkansas for Medical Sciences, Little Rock, Arkansas 72205, USA.

Ibogaine (IBO) is an indole alkaloid from the West African shrub, Tabernanthe iboga. It is structurally related to harmaline, and both these compounds are rigid analogs of melatonin. IBO has both psychoactive and stimulant properties. In single-blind trials with humans, it ameliorated withdrawal symptoms and interrupted the addiction process. However, IBO also produced neurodegeneration of Purkinje cells and gliosis of Bergmann astrocytes in the cerebella of rats given even a single dose (100 mg/kg, ip). Here, we treated rats (n = 6 per group) with either a single ip injection of saline or with 25 mg/kg, 50 mg/kg, 75 mg/kg, or 100 mg/kg of IBO. As biomarkers of cerebellar neurotoxicity, we specifically labeled degenerating neurons and axons with silver, astrocytes with antisera to glial fibrillary acidic protein (GFAP), and Purkinje neurons with antisera to calbindin. All rats of the 100-mg/kg group showed the same pattern of cerebellar damage previously described: multiple bands of degenerating Purkinje neurons. All rats of the 75-mg/kg group had neurodegeneration similar to the 100-mg/kg group, but the bands appeared to be narrower. Only 2 of 6 rats that received 50 mg/kg were affected, despite few degenerating neuronal perikarya, cerebellar from these rats did contain patches of astrocytosis similar to those observed with 75 or 100 mg/kg IBO. These observations affirm the usefulness of GFAP immunohistochemistry as a sensitive biomarker of neurotoxicity. None of the sections from the 25-mg/kg rats, however stained, were distinguishable from saline controls, indicating that this dose level may be considered as a no-observable-adverse-effect level (NOAEL).

PMID: 10966515 [PubMed - indexed for MEDLINE]
Xu et al. accomplished research in part at the National Center for Toxicological Research an FDA laboratory. The research demonstrated no neurotoxicity in rats at 25 mg/kg.

Other research indicated no evidence of neurotoxicity in the primate and mouse, and postmortem neuropathological examination in a woman treated with up to 30 mg/kg.
Mechanisms of antiaddictive actions of ibogaine.

Glick SD, Maisonneuve IS.

Department of Pharmacology and Neuroscience, Albany Medical College, New York 12208, USA.
sglick@ecgateway.amc.edu

Ibogaine, an alkaloid extracted from Tabernanthe iboga, is being studied as a potential long-acting treatment for opioid and stimulant abuse as well as for alcoholism and smoking. Studies in this laboratory have used animal models to characterize ibogaine's interactions with drugs of abuse, and to investigate the mechanisms responsible. Ibogaine, as well as its metabolite, noribogaine, can decrease both morphine and cocaine self-administration for several days in some rats; shorter-lasting effects appear to occur on ethanol and nicotine intake. Acutely, both ibogaine and noribogaine decrease extracellular levels of dopamine in the nucleus accumbens of rat brain. Ibogaine pretreatment (19 hours beforehand) blocks morphine-induced dopamine release and morphine-induced locomotor hyperactivity while, in contrast, it enhances similar effects of stimulants (cocaine and amphetamine). Ibogaine pretreatment also blocks nicotine-induced dopamine release. Both ibogaine and noribogaine bind to kappa opioid and N-methyl-D-aspartate (NMDA) receptors and to serotonin uptake sites; ibogaine also binds to sigma-2 and nicotinic receptors. The relative contributions of these actions are being assessed. Our ongoing studies in rats suggest that kappa agonist and NMDA antagonist actions contribute to ibogaine's effects on opioid and stimulant self-administration, while the serotonergic actions may be more important for ibogaine-induced decreases in alcohol intake. A nicotinic antagonist action may mediate ibogaine-induced reduction of nicotine preferences in rats. A sigma-2 action of ibogaine appears to mediate its neurotoxicity. Some effects of ibogaine (e.g., on morphine and cocaine self-administration, morphine-induced hyperactivity, cocaine-induced increases in nucleus accumbens dopamine) are mimicked by kappa agonist (U50,488) and/or a NMDA antagonist (MK-801). Moreover, a combination of a kappa agonist and a NMDA agonist will partially reverse several of ibogaine's effects. Ibogaine's long-term effects may be mediated by slow release from fat tissue (where ibogaine is sequestered) and conversion to noribogaine. Different receptors, or combinations of receptors, may mediate interactions of ibogaine with different drugs of abuse.
Review of the use of ibogaine outside of the African Bwiti religious context

Alper KR, Lotsof HS, Kaplan CD.

Department of Psychiatry, New York University School of Medicine, New York, NY 10016, USA; Department of Neurology, New York University School of Medicine, New York, NY 10016, USA.

AIM OF THE STUDY: Ibogaine is a naturally occurring psychoactive indole alkaloid that is used to treat substance-related disorders in a global medical subculture, and is of interest as an ethnopharmacological prototype for experimental investigation and possible rational pharmaceutical development. The subculture is also significant for risks due to the lack of clinical and pharmaceutical standards. This study describes the ibogaine medical subculture and presents quantitative data regarding treatment and the purpose for which individuals have taken ibogaine. MATERIALS AND METHODS: All identified ibogaine "scenes" (defined as a provider in an associated setting) apart from the Bwiti religion in Africa were studied with intensive interviewing, review of the grey literature including the Internet, and the systematic collection of quantitative data. RESULTS: Analysis of ethnographic data yielded a typology of ibogaine scenes, "medical model", "lay provider/treatment guide", "activist/self-help", and "religious/spiritual". An estimated 3414 individuals had taken ibogaine as of February 2005, a fourfold increase relative to 5 years earlier, with 66% of the total having taken it for the treatment of a substance-related disorder, and 53% specifically for opioid withdrawal. CONCLUSIONS: Opioid withdrawal is the most common reason for which individuals took ibogaine. The focus on opioid withdrawal in the ibogaine subculture distinguishes ibogaine from other agents commonly termed "psychedelics", and is consistent with experimental research and case series evidence indicating a significant pharmacologically mediated effect of ibogaine in opioid withdrawal.
Ibogaine science continues to grow providing 100s of peer reviewed papers
Ibogaine: Multiple mechanisms of action & receptor system effects where drugs of abuse also show activity

- Dopamine
- Opiate
- Serotonin
- NMDA (N-methyl-D-aspartic acid)

- Nicotinic
- GDNF (Glial cell derived neurotrophic factor)
- Signal transduction independent of receptor binding
The objective of the pharmaceutical industry is to return profit to corporate shareholders

This greatly affects the selection of compounds and indications for drug development, and tends to discourage the development of innovative drugs to treat addiction.
NIDA has focused on already existing drugs which are then developed for addiction as a new indication, and not the development of fundamentally new pharmacological strategies such as ibogaine.
NIDA director signs agreement to develop buprenorphine 1994
NIDA says “NO” to funding clinical development of ibogaine 1995
In 2004 NIDA makes available under the Freedom of Information Act (FOIA) a Drug Master File (DMF) provided to FDA comprising 16 volumes of data of approximately 4,000 pages.
Partial list of broad-ranging studies in FDA Drug Master File (DMF) included in 16 volumes of data submitted by US National Institute on Drug Abuse (NIDA) for ibogaine.

• Acute Oral Toxicity Study of Ibogaine HCl in Rats.
• 32 Day Range-Finding Study of Ibogaine in Rats.
• Dose Response Neurotoxicity Study of Ibogaine in Rats.
• Dose Response Effect of Ibogaine on Analgesia and Mortality in Morphine-Dependent Rats.
• Pharmacokinetic Studies of Treatment Drugs Ibogaine.
• 14 Day Dose Range-Finding Toxicity Study of Ibogaine HCl in Dogs.
• Acute Neurotoxicity Study of Ibogaine HCl in Dogs.
• Salmonella/Mammalian-Microsome Plate Incorporation Mutagenicity Assay (AMES Test).
• L5178Y/TK +/- Moue Lymphoma Mutagenesis Assay
Among the 16 volumes of data are mutagenicity studies showing ibogaine not to be a thalidomide-like drug.

**SALMONELLA/MAMMALIAN-MICROSOME PLATE INCORPORATION MUTAGENICITY ASSAY (AMES TEST)**

**FINAL REPORT**

Sponsor: National Institute on Drug Abuse
Medical Development Division
Parklawn Building, Room 11A-55
5600 Fishers Lane
Rockville, MD 20857

Mutagenicity Assay

The results of the mutagenicity assay are presented in Tables 2 through 11 and summarized in Table 12. These data were generated in Experiment B1. Neither precipitate nor appreciable toxicity was observed.

In Experiment B1, no positive responses were observed with any of the tester strains in the presence and absence of S9 activation.

All criteria for a valid study were met as described in the protocol.

**CONCLUSION**

The results of the Salmonella/Mammalian-Microsome Plate Incorporation Mutagenicity Assay indicate that under the conditions of this study, National Institute on Drug Abuse, Medical Development Division's test article ibogaine hydrochloride did not cause a positive response with any of the tester strains in the presence and absence of Aroclor-induced rat liver S9.
Comparative safety perspectives
Drug-related fatalities (d-rf)

• Ibogaine/iboga (1989-2006) 11 d-rf
• Methadone (2004) (USA) 3965 d-rf
• FDA approved drugs in US hospitals (1999) 112,000 d-rf
Drug-related fatalities/treatment episodes

• Ibogaine/iboga (all known treatment episodes [TEs] 1989-2006): 11 fatalities in 3,414 TEs (1 ibogaine-related death/427 TEs)¹

• Methadone (Australia 2000-2003; national registration data): 282 methadone-related death in 102,615 TEs (1 methadone-related death /364 TEs)²

• Methadone (Utah 2004; Controlled substance and medical examiner data bases): 110 fatalities in which medical examiner made mention of methadone in attribution of cause of death, 52,350 methadone prescriptions (1 methadone-related death /476 methadone prescriptions)³

Ibogaine Activist
Advocacy Organizations Play Role in Ibogaine Development

- International Coalition for Addict Self-Help (ICASH) 1989
- Dutch Addict Self-Help (DASH) 1990
- Cures-Not Wars (ibogaine and other issues) 1994
- Freedomroot Ibogaine Underground 2004
ICASH logo

Used to attract attention of government officials and media
Nico Adriaans was one of the founders of both the Rotterdam Junkies Union and Dutch Addict Self-Help (DASH), and the first needle exchange in 1981. DASH was an ibogaine self-help organization that petitioned the Dutch government and organized drug users to demand ibogaine availability. DASH provided ibogaine at no cost to heroin users.
ICASH Organizing in the US
Cures-Not-Wars placed pressure on NIDA to support Ibogaine research through protests
Mindvox internet ibogaine list (user advocacy continues)

“We all got to help each other best we can. No one else gives a shit ‘bout us hippy freak junkies? ”

anon.

To join send an email to
ibogaine-subscribe@mindvox.com
Ibogaine underground appears 2004

“Freedomroot”

“FM- ... We feel that continuing the focus offshore, outside the US, has not served a majority of people inside the US. Like many other grassroots movements, which facilitated change, treatments, sessions, need to be done where they belong, in all major US cities, as cost effectively as possible. “

http://www.drugwar.com/ibonytc.shtm
Ibogaine represents both harm reduction and demand reduction.

DEA desk officer in the Netherlands asks how the Dutch are allowing a demand reduction drug like ibogaine to be researched in the Netherlands?

Ibogaine proponents view the drug as significant harm reduction tool and basis for political action.
Stigma

A mark of disgrace associated with a particular circumstance, quality or person: for instance the stigma of chemical dependence.
Ibogaine Effects on Stigma

Ibogaine has the ability to remove the stigmatized condition, transforming the patient to a state often described as a preaddictive. The transformation of a stigmatized person into one who is not stigmatized will affect the individual, allowing a greater contribution to self and society, improving quality of life issues.
Why ibogaine is not available

1. Industry deems ibogaine not to be profitable.
2. The molecule is found in nature and cannot be owned.
3. Stigmatized patient population with liability higher than general population due to a greater mortality rate.
4. Government, industry and academia chose to place their interest to treat narcotic dependence in the development of opioid drugs with which they are familiar.
5. Ibogaine represents a new scientific paradigm to the understanding of addiction. New technologies are resisted.
7. Abandonment of FDA study by academic professionals to establish a for-profit clinic.
Paths to ibogaine availability

1. Pharmaceutical company or government agency prepared to finance regulatory development.

2. Supplies of pharmaceutical grade ibogaine.

3. Grassroots constituency demanding availability of ibogaine.

4. Political advocacy movement to pressure government and industry into action.

5. A scientific community supporting ibogaine research.
Why ibogaine should be available

1. Ibogaine significantly reduces withdrawal
2. Interrupts drug craving
3. Returning patients to a preaddictive state
4. Eliminates stigma
5. Returns free choice
Its in your hands now!
Activism, advocacy and science
Patient rights - User rights