



THE LITTLE BOOK OF
**PSYCHEDELIC
SUBSTANCES**



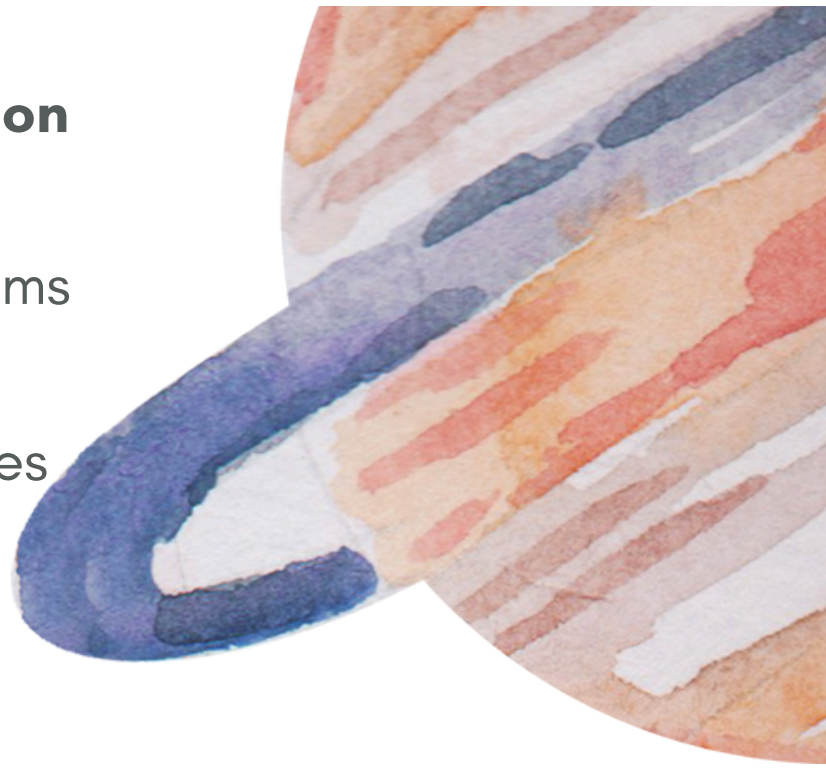
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NOW WE'RE READY
FOR LIFT OFF!

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PSILOCYBIN

4-PHOSPHORYLOXY-N,N-DIMETHYLTRYPTAMINE

Psilocybin is a naturally occurring tryptamine alkaloid found in upwards of 200 species of fungi. When consumed, the body rapidly metabolizes psilocybin to psilocin which activates serotonin 2A (5-HT_{2A}) receptors and profoundly changes consciousness for 3-6 hours. Psilocybin is a classical psychedelic characterized by visual distortions, heightened bodily sensations, colorful visions, altered auditory perceptions, synesthesia, strong emotions, hallucinations, and spatial and cognitive shifts in relation to space and time.

BRAND NAME: none

CHEMICAL NAME:

4-phosphoryloxy-N,N-dimethyltryptamine

DRUG CLASSIFICATION: classic
psychedelic

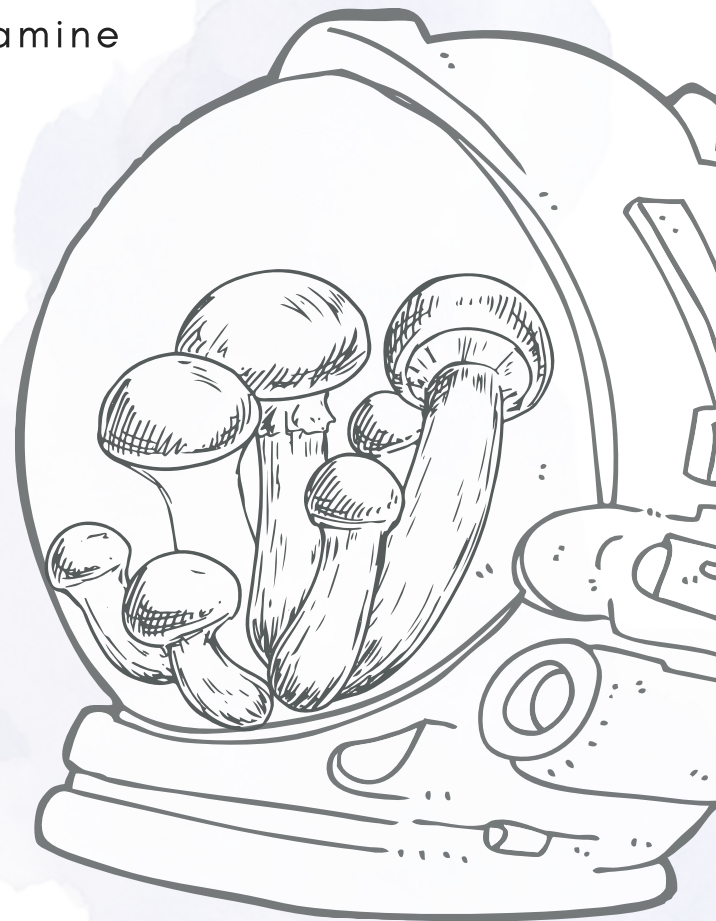
DRUG TYPE: psilocybin (synthetic),
psilocybin-containing fungi

LEGAL STATUS: illegal in most
countries

CONTROLLED SUBSTANCE (USA):
Schedule I

CLINICAL TRIAL SPONSORS

- [Usona Institute](#)
- [COMPASS Pathways](#)
- [Heffter Institute](#)
- [Beckley Foundation](#)
- University investigator-initiated studies
- Many new companies



PSILOCYBIN

CLINICAL & THERAPEUTICS

Synthetic psilocybin is under investigation in clinical trials in the United States and Europe for several health conditions. The FDA granted Breakthrough Therapy designations for psilocybin therapy for both treatment-resistant depression and major depressive disorder. A Breakthrough Therapy designation can quicken regulatory approval timelines for novel therapeutics that show better performance than available medications for life-threatening conditions. Psilocybin clinical trials are ongoing with FDA marketing approval possible in 2024 or later.

POSITIVE EFFECTS

- Visual distortions
- Vivid imagery with eyes open or closed
- Auditory and visual hallucinations
- Sensory synthesis
- Feelings of expansiveness
- Feelings of oneness and connection with others and the universe
- Heightened emotions
- Transcendence of space and time
- Ego dissolution
- Mystical experiences
- Altered cognition
- Introspection and insightfulness

NEGATIVE EFFECTS

- Panic attacks, anxiety, or confusion
- Paranoia
- Dysphoria
- Irrational and reckless behavior
- Impaired concentration and focus, disordered thinking
- Dizziness
- Disorientation
- Restlessness
- Muscle weakness
- Nausea or vomiting
- Light sensitivity
- Pupil dilation
- Flashbacks



4-PHOSPHORYLOXY-N,N-DIMETHYLTRYPTAMINE

PSILOCYBIN

CLINICAL & THERAPEUTICS

INDICATIONS UNDER STUDY FOR PSILOCYBIN

- Major depressive disorder
- Treatment-resistant depression
- Anxiety and depression in cancer patients
- Depression in people with mild cognitive impairment or early Alzheimer's disease
- Type 2 Bipolar Disorder depression
- Nicotine dependence
- Alcohol use disorder
- Substance use disorders (cocaine, opioid)
- Co-occurring depression and alcohol use disorder
- Cluster, migraine, and post-traumatic headache disorders
- Anorexia nervosa
- Obsessive compulsive disorder
- Demoralization in AIDS/HIV survivors

In most countries of the world, possession and use of psilocybin mushrooms are illegal. However, psilocybin retreats are operating legally in a few countries such as Jamaica and the Netherlands. In May 2019, Denver Colorado became the first US city to decriminalize psilocybin mushrooms followed shortly after by Oakland, Santa Cruz, Ann Arbor, Washington DC, and the state of Oregon.

MECHANISMS OF ACTION

- High-affinity agonist at serotonin 2A (5-HT_{2A}) receptors, the primary target for subjective effects
- Agonist at 5-HT_{2C}, 5-HT_{1A}, and 5-HT_{1B} receptors
- Modulation of serotonergic, dopaminergic, and glutamatergic systems

4-PHOSPHORYLOXY-N,N-DIMETHYLTRYPTAMINE

PSILOCYBIN

CLINICAL & THERAPEUTICS

The psilocybin experience can be metaphorically likened to a journey. During the journey, the person can visit places deep within the recesses of their own mind, have out-of-body experiences where they venture to far away universes to meet celestial beings, or even engage in conversations with loved ones long since passed. The range of possible experiences is infinite and dose-dependent. A person's mental state and the environment where psilocybin is taken affect the subjective and emotional experience.

THERAPEUTIC APPROACH

- Co-therapy team of two trained guides/therapists deliver the treatment
- 1 - 4 preparatory sessions
- 1 - 4 psilocybin sessions, spaced weeks to months apart
- Comfortable living room like setting, participant listens to music and wears eye shades
- Follow-up integration sessions OR follow-up safety/efficacy assessments
- Therapeutic approaches vary widely, some include motivational enhancement therapy and various degrees of psychotherapy while others include psychological support with very little preparation/integration therapy

DOSING IN CLINICAL TRIALS

- Oral (capsule)
- Very low dose (1-9 mg psilocybin)
- Low dose (10-19 mg psilocybin)
- Medium dose (20-29 mg psilocybin)
- High dose (>30 mg psilocybin)
- Duration of effects 3-6 hours

SAFETY & TOLERABILITY

- Well tolerated in individuals screened for specific physiological and psychological health criteria
- Increases or decreases in blood pressure and heart rate
- Low potential for dependence in medical and non-medical settings
- Common adverse reactions: anxiety, psychological distress, paranoid ideation, physical discomfort, headache, nausea

4-PHOSPHORYLOXY-N,N-DIMETHYLTRYPTAMINE

PSILOCYBIN

NON-MEDICAL USES

Psilocybin-containing mushrooms have been revered in ceremonial spaces dating back thousands of years in indigenous cultures, and are still traditionally used by some indigenous communities in Mexico. With the discovery of LSD, research into psychedelic compounds and their applications in psychiatric medicine blossomed. Psilocybin was investigated for therapeutic benefits throughout the 1960s and gained precedence in Western cultures when it was popularized among the hippie counterculture. The 1970s Controlled Substance Act made psilocybin a Schedule I substance where it resides today.

COMMON STREET NAMES

- Psilocybin mushrooms or fungi
- Magic mushrooms
- Psychedelic mushrooms
- Caps
- Mushies
- Shrooms
- Fungus
- Buttons
- Alice

ROUTES OF ADMINISTRATION

- Oral (dried or fresh mushrooms)
- Oral (synthetic psilocybin)

POPULAR SETTINGS

- Home
- Natural environments
- Electronic music festivals
- House parties
- Concerts
- Art festivals

COMMON MUSHROOM PREPARATIONS

- Teas
- Chocolates
- Crushed into a powder (edibles or used to fill capsules)
- Lemon tek

4-PHOSPHORYLOXY-N,N-DIMETHYLTRYPTAMINE

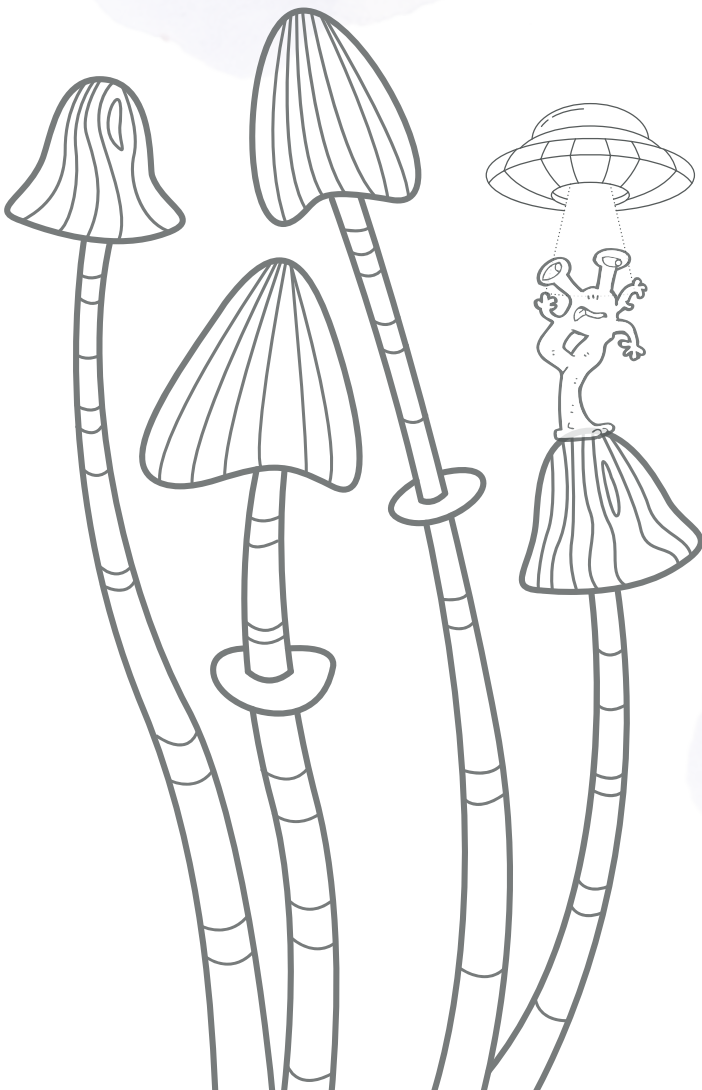
PSILOCYBIN

NON-MEDICAL USES

COMMON PSILOCYBIN DOSES*

- Microdose: 0.1 - 0.5 grams
- Low dose: 0.5 - 2 grams
- Moderate dose: 2 - 4 grams
- High dose: >4 grams

*Potency varies across different mushroom species



PRIMARY RISKS

- Misidentification of mushrooms
- Mushrooms contaminated with molds or toxins
- Physical harms caused by changes in judgement and dangerous behaviors
- Complications with pre-existing health conditions
- Flashbacks

FACTORS AFFECTING RISK PROFILE

- Dose
- Mushroom sourcing
- Pre-existing health conditions
- Set and setting

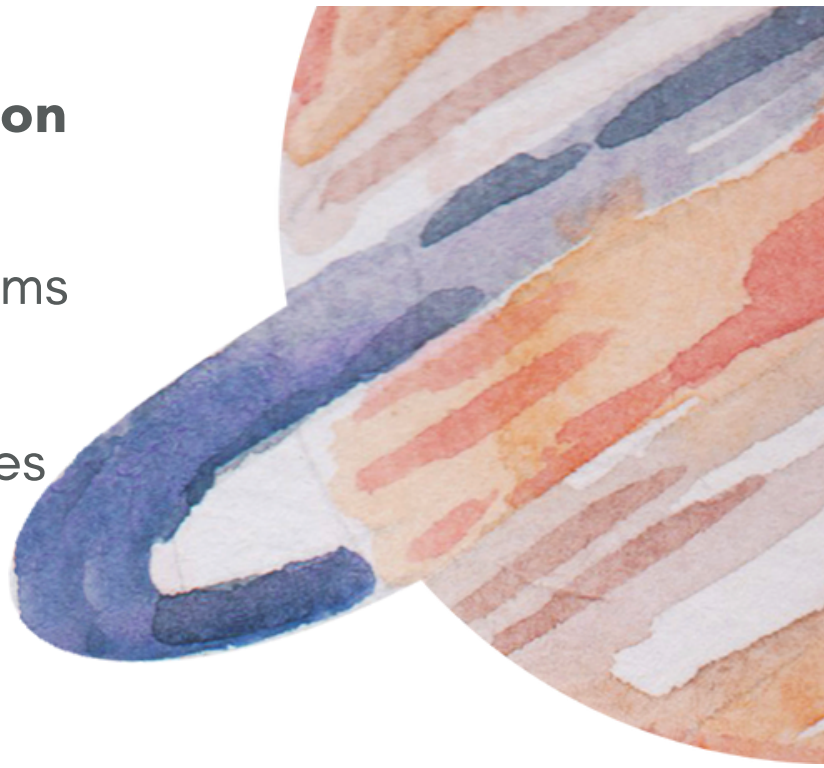
4-PHOSPHORYLOXY-N,N-DIMETHYLTRYPTAMINE

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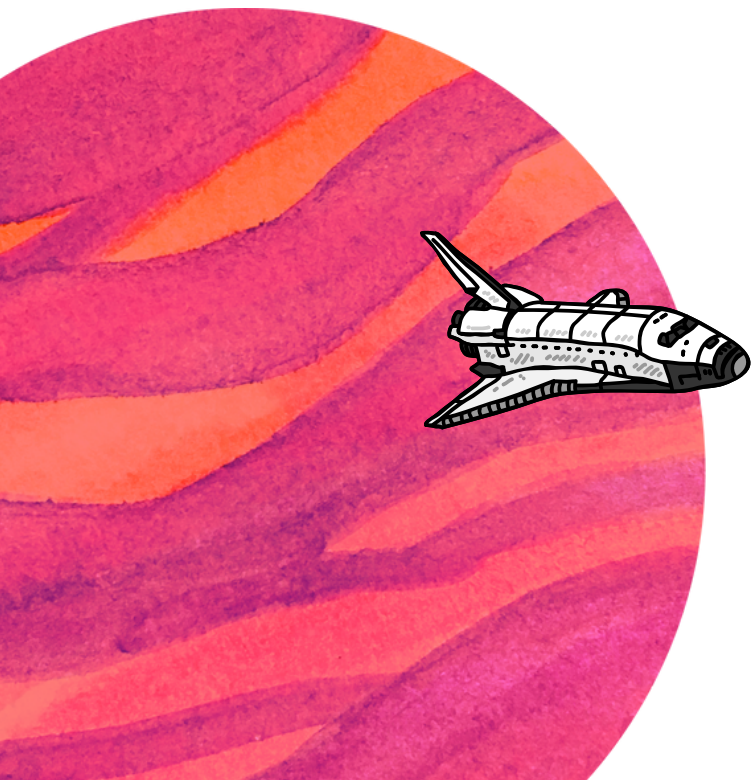


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MDMA

3,4-METHYLENEDIOXYMETHAMPHETAMINE

MDMA is an amphetamine derivative classified as an entactogen or empathogen. MDMA induces psychoactive effects of heightened emotions, openness, boundless love, and feelings of oneness and connection to others and the universe. MDMA stimulates the release of neurotransmitters (serotonin, dopamine, and norepinephrine) and hormones (oxytocin, vasopressin, cortisol, and prolactin). These neurochemicals dynamically interact to induce mind-altering effects and increase blood pressure, body temperature, and heart rate. MDMA, also known as Ecstasy and Molly, has been a popular party drug since the early 1980s and is classified as a Schedule I controlled substance in the US.

BRAND NAME: none

CHEMICAL NAME: 3,4-methylenedioxyamphetamine (MDMA)

DRUG CLASSIFICATION:

empathogen/entactogen

DRUG TYPE: synthetic

LEGAL STATUS: illegal world-wide

CONTROLLED SUBSTANCE (USA):
Schedule I

CLINICAL TRIAL SPONSORS

- [MAPS / MAPS PBC](#)
- [MindMed](#)
- University investigator-initiated studies



MDMA

CLINICAL & THERAPEUTICS

MDMA-assisted psychotherapy is under investigation in clinical trials for treating several mental health disorders. In a clinical setting with trained therapists, a person undergoing MDMA treatment is first prepared for the experience in 90-minute therapy sessions before embarking in all-day MDMA-assisted psychotherapy sessions (2-3 sessions, spaced 1 month apart). The therapeutic process continues in follow-up integration sessions where the person reflects on the journey, stabilizes insights, and establishes a plan for their healing to continue outside the therapy room.

POSITIVE EFFECTS

- Euphoria
- Heightened awareness and sensory perceptions
- Feelings of expansiveness
- Feelings of oneness and connection with others and the universe
- Increased energy and alertness
- Empathy

NEGATIVE EFFECTS

- Panic attacks, anxiety, or confusion
- Nausea or vomiting
- Muscle tension, tremors, shaking
- Sweating
- Blurred vision
- Teeth grinding, jaw tightness
- Moderate potential for addiction or problematic use in non-medical settings

INDICATIONS UNDER STUDY FOR MDMA-ASSISTED PSYCHOTHERAPY

- Posttraumatic stress disorder (PTSD)
- Anxiety related to a life-threatening illness
- Social anxiety in autistic adults
- Anorexia nervosa
- Binge eating disorder
- Alcohol use disorder

MECHANISMS OF ACTION

- Binds to and reverses transporter proteins (SERT, NET, DAT)
- Increase release of serotonin, norepinephrine, and dopamine
- Increases release of hormones - oxytocin, vasopressin, prolactin, and cortisol

MDMA

CLINICAL & THERAPEUTICS

THERAPEUTIC APPROACH (MAPS)

- Co-therapy team of two trained health providers deliver the treatment
- Three 90-minute preparatory sessions
- Three 8-hour MDMA-assisted psychotherapy sessions, spaced a month apart
- Three integration sessions following each MDMA session

DOSING IN CLINICAL TRIALS

- Oral
- Initial dose 75-125 mg MDMA
- Supplemental dose equal to half the initial dose (37.5 - 62.5 mg MDMA) given two hours later
- Duration of effects 6-8 hours

SAFETY & TOLERABILITY

- Well tolerated in individuals screened for specific physiological and psychological health criteria
- Increases in blood pressure, heart rate, and body temperature similar to moderate exercise
- Low potential for abuse in medically supervised administrations
- Common adverse reactions (reported by >40% in phase 1 MDMA studies): difficulty concentrating, dizziness, dry mouth, feeling cold, impaired balance/gait, jaw clenching/tight jaw, lack of appetite, restless legs, restlessness, and thirst

In 2017, the FDA granted a Breakthrough Therapy designation for MDMA-assisted psychotherapy for the treatment of PTSD.

Preliminary evidence showed MDMA was a substantial improvement over available PTSD medications (SSRIs). Clinical trials are now in the last phase of testing (phase 3). If significant, MDMA could become approved for the treatment of PTSD by 2023.



MDMA

NON-MEDICAL USES

COMMON STREET NAMES

- Ecstasy
- E, X, and XTC
- Molly
- Love drug
- ADAM
- Beans
- Disco biscuits

POPULAR SETTINGS

- Home
- Natural environments
- Nightclubs
- Electronic music festivals
- Raves
- Concerts
- House parties
- Art festivals

ROUTES OF ADMINISTRATION

- Oral (most common)
- Snorted
- Rectal
- Injected
- Smoked

Pressed tablets, powder, capsules

ORAL DOSING IN NON-MEDICAL SETTINGS

- Low dose: 60-80 mg
- Moderate dose: 81-130 mg
- High dose: 131 - 200 mg
- Very high dose: >200 mg

PRIMARY RISKS

- Dehydration or overhydration, both can cause complications when a person has taken MDMA
- Interactions of MDMA with other drugs or medications
- Complications with pre-existing health conditions

FACTORS AFFECTING RISK PROFILE

- Dose
- Frequency of dosing
- Contamination of drug source or polydrug/medication use
- Pre-existing disease or health conditions
- Ambient temperature
- Activity level
- Fluid intake



KETAMINE

2-(2-CHLOROPHENYL)-2-(METHYLAMINO)-CYCLOHEXANONE

Discovered in 1962 and patented in 1963, racemic ketamine is an arylcyclohexylamine used as a rapid-acting general anesthetic agent in human and veterinary medicine. The FDA approved ketamine in 1970 as an anesthetic drug and is now legally prescribed off-label for a growing list of indications. Ketamine is a non-competitive NMDA antagonist and interacts with a number of other receptor targets that contribute to its effects.

BRAND NAME: Ketalar

CHEMICAL NAME:

2-(2-chlorophenyl)-2-(methylamino)-cyclohexanone

DRUG CLASSIFICATION: dissociative

DRUG TYPE: synthetic

LEGAL STATUS: legal with a medical prescription when clinically indicated

CONTROLLED SUBSTANCE (USA):

Schedule III

CLINICAL TRIAL SPONSORS

- University investigator-initiated studies
- Ketamine Research Foundation
- Janssen

DRUG NAME/COMPANY

- Ketalar / Par Sterile Products
- Ketamine hydrochloride / Mylan Institutional
- Ketamine hydrochloride / Hospira
- Ketamine hydrochloride / West-Ward Pharms Int



KETAMINE

CLINICAL & THERAPEUTICS

Beyond its primary application for anesthesia, ketamine is used as an analgesic, anti-obsessional, and antidepressant compound, and possesses neuroprotective and neuroplastic properties. The effects of ketamine are highly dependent on the bioavailable dose by way of the route of administration, ranging from slight perceptual disruptions to paralysis and full dissociation to sedation. In medical settings, ketamine is considered relatively safe because it has less circulatory and respiratory depression compared to other anesthetic agents. Long-term use and high doses of ketamine are associated with greater incidence of adverse effects and increased risk of dependence.

POSITIVE EFFECTS

- Drowsiness
- Dissociative (body dissociates from the mind)
- Out-of-body experiences
- Changes in perception, cognition, and emotion
- Vivid imagery, visual hallucinations
- Mood enhancement
- Ego dissolution
- Transcendence of space and time
- Mystical experiences
- Experiences of death and rebirth
- Muscle relaxation
- Pain relief
- Feeling of awe and wonder

ACUTE NEGATIVE EFFECTS

- Anxiety
- Drowsiness
- Paranoid delusions
- Dysphoria
- Distorted perceptions of body and self
- Loss of coordination
- Disorientation
- Confusion
- Muscle trembles or jerks
- Psychotic episodes
- Accidents (falling, car, etc)
- Psychological distress
- Loss of airway function

KETAMINE

CLINICAL & THERAPEUTICS

NEGATIVE EFFECTS OF PROLONGED USE

- Kidney and bladder (cystitis) toxicity
- Urinary tract dysfunction
- Physical and psychological dependence
- Misuse, tolerance, and addiction
- Withdrawal syndrome
- Flashbacks

APPROVED INDICATIONS

- Anesthetic compound for diagnostic and surgical procedures

COMMON OFF-LABEL INDICATIONS

- Pain
 - Major depression disorder
 - Mood disorders
 - Addiction disorders*
 - Posttraumatic stress disorder*
- *Experimental, caution warranted

MECHANISMS OF ACTION

- N-methyl-D-aspartate NMDA receptor antagonist (blocks excitatory signalling of glutamate)
- Direct and/or indirect effects at opioid, monoaminergic, cannabinoid, nitric oxide, muscarinic, nicotinic, and sigma receptors
- Neuroprotective properties, promotes neuroplasticity

Ketamine is only FDA approved for use as an anesthetic agent. However, the last 10 years have brought an increase in off-label prescriptions for pain management and mental health conditions (major depressive disorder, OCD, suicidal ideation, and others), meaning rigorous controlled trials to gain FDA approval have not been conducted (except for esketamine, see next section). It's increasingly used to reduce depression symptoms and improve mood. Some clinicians administer ketamine to treat PTSD and substance use disorders, although use for these indications is experimental and warrants caution. Individuals who have substance use disorders can be more vulnerable to become ketamine dependent; those with PTSD may have traumatic memories resurface. Without proper support, these experiences can be harmful rather than therapeutic. Research in controlled clinical trials is necessary to establish safety profiles, dosing, and efficacy for each psychiatric indication.

2-(2-CHLOROPHENYL)-2-(METHYLAMINO)-CYCLOHEXANONE

KETAMINE

CLINICAL & THERAPEUTICS

The use of ketamine for mental health symptoms falls into two broad frameworks - pharmaceutical/biochemical and ketamine-assisted psychotherapy (KAP). Ketamine itself has physiological effects that appear important for antidepressant and other therapeutic effects. Some doctors will administer ketamine, typically through IV infusions or lozenges, to relieve psychiatric symptoms. In this framework, the drug itself acts through neurobiological mechanisms and the symptom relief is dependent on repeated administrations because the therapeutic effects last for days or up to two weeks. Patients are offered minimal support and no talk therapy which may lead to a dependence on ketamine to achieve symptom reduction. Long-term use of ketamine is associated with negative side effects, namely kidney and bladder toxicity and ketamine tolerance and dependence.

ROUTES OF ADMINISTRATION

- Oral
- Sublingual/transbuccal
- Intranasal
- Rectal
- Subcutaneous
- Intramuscular (IM)
- Intravenous (IV)
- Onset and duration of effects dependent on route

DOSING*

Intravenous (IV)

- 0.5 mg/kg over a 40 minute infusion
- Dose for Induction of anesthesia: 1.0 - 4.5 mg/kg
- Onset of effects 45 seconds (IV)

Intramuscular (IM)

- For anxiolysis or analgesia:
- Low dose: 0.25 - 0.5 mg/kg
- Moderate dose: 0.5 - 1.0 mg/kg
- To induce psychedelic effects:
- High dose: 1.0 - 2.0 mg/kg
- Dose for Induction of anesthesia: 6.5 - 13.0 mg/kg
- Onset of effects 3 mins, Duration of effects 75 mins, sessions last 2-4 hours

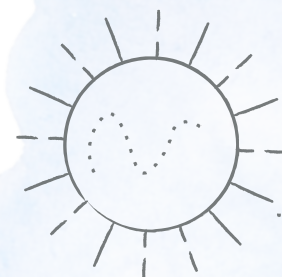
Nasal

- 25-300 mg

Lozenge

- Transbuccal and/or sublingual absorption
- 50-300 mg

*Dosing varies depending on route of administration and desired effects



KETAMINE

CLINICAL & THERAPEUTICS

Ketamine-assisted psychotherapy (KAP) is a method where low to moderate doses of ketamine are delivered with the intention of altering consciousness to facilitate psychotherapy. A therapist sits and talks with a client as they experience ketamine. Alternatively, high doses of ketamine are used to induce a non-ordinary state of consciousness where a person experiences major shifts of perceptions in many ways similar to classical psychedelics. Mystical-type experiences and feelings of ego dissolution are common for high dose sessions. These effects can be extremely negative if a person is not well prepared and supported during and afterwards.

KETAMINE-ASSISTED PSYCHOTHERAPY

- Trained therapeutic provider delivers the treatment, qualified medical professionals prescribe ketamine off-label
- Preparatory psychotherapy sessions
- Ketamine administration session with psychological support and psychotherapy during and after
- Integration sessions following each ketamine session

SAFETY & TOLERABILITY

- Well tolerated in individuals screened for specific physiological and psychological health criteria
- Dose and frequency of use affects risk profile

Either immediately after the effects of ketamine dissipate and/or in the days to weeks to follow, a person undergoes a course of counseling or psychotherapy to examine the experience and emotions within the framework of their personal goals. The psychotherapeutic process aims to stabilize positive behavioral changes, consolidate psychological material, resolve psychological issues, improve relationships, catalyze new insights, and enhance self-awareness. While still under-researched, ketamine-assisted psychotherapy is presumed to amplify the neurobiological properties of ketamine by addressing underlying psychological issues and bolstering transformational healing.

KETAMINE

NON-MEDICAL USES

Similar to other classical psychedelics, not everyone is the right fit for ketamine, especially at higher doses. Screening for contraindicated medical and mental health conditions is essential as is a proper setting for psychological safety. Research dating back to the 1950s and current day psychedelic-assisted clinical trials are elucidating how psychedelic experiences can be beneficial for therapeutic applications, and what parameters are necessary to support a person undergoing these experiences.

WANT TO LEARN MORE ABOUT ETHICAL GUIDELINES IN ADMINISTERING KETAMINE-ASSISTED THERAPY? CHECK OUT [KETAMINE GUIDELINES FOR CLINICIANS AND MORE FROM KRIYA INSTITUTE.](#)

COMMON STREET NAMES

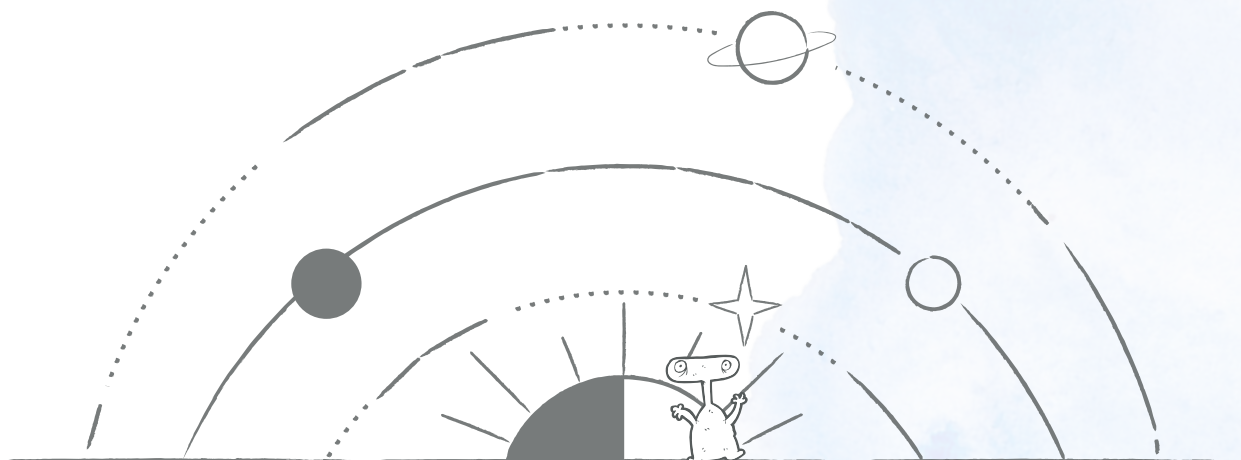
- Ketamine
- K
- Special K
- Kit kat
- Cat tranquilizer
- Vitamin K

POPULAR SETTINGS

- Nightclubs
- Discotheques
- Raves
- House parties
- Electronic music festivals
- Home

ROUTES OF ADMINISTRATION

- Nasal
- Transbuccal
- Sublingual
- Intravenous
- Intramuscular
- Rectal



2-(2-CHLOROPHENYL)-2-(METHYLAMINO)-CYCLOHEXANONE

KETAMINE

NON-MEDICAL USES

DOSING

Dosing and effects are dependent on the route of administration. Ketamine is administered in liquid or powder form. See clinical section for dosing examples.

PRIMARY RISKS

- Accidents
- Misuse, dependence, and addiction
- Pre-existing health conditions where a significant elevation of blood pressure would be hazardous
- Impaired memory and mood swings
- Flashbacks
- Bladder, kidney, and heart toxicity
- Sexual assaults
- Respiratory depression when mixed with alcohol, GHB, or opioids

*Risks of very high doses: elevated heart rate, hypertension, seizures, coma, death, stroke, respiratory distress, asphyxiation, and psychological distress

FACTORS AFFECTING RISK PROFILE

- Pre-existing health conditions
- Hypersensitivity to ketamine
- Duration and frequency of use
- Dose
- Psychological history
- History of trauma
- Mixing ketamine with other substances (alcohol and GHB)

2-(2-CHLOROPHENYL)-2-(METHYLAMINO)-CYCLOHEXANONE

ESKETAMINE

2-(2-CHLOROPHENYL)-2-(METHYLAMINO)-CYCLOHEXANONE

BRAND NAME: Spravato

GENERIC NAME: S-ketamine
hydrochloride

CHEMICAL NAME: 2-(2-chlorophenyl)-2-(methylamino)-cyclohexanone

DRUG CLASSIFICATION:

disassociative

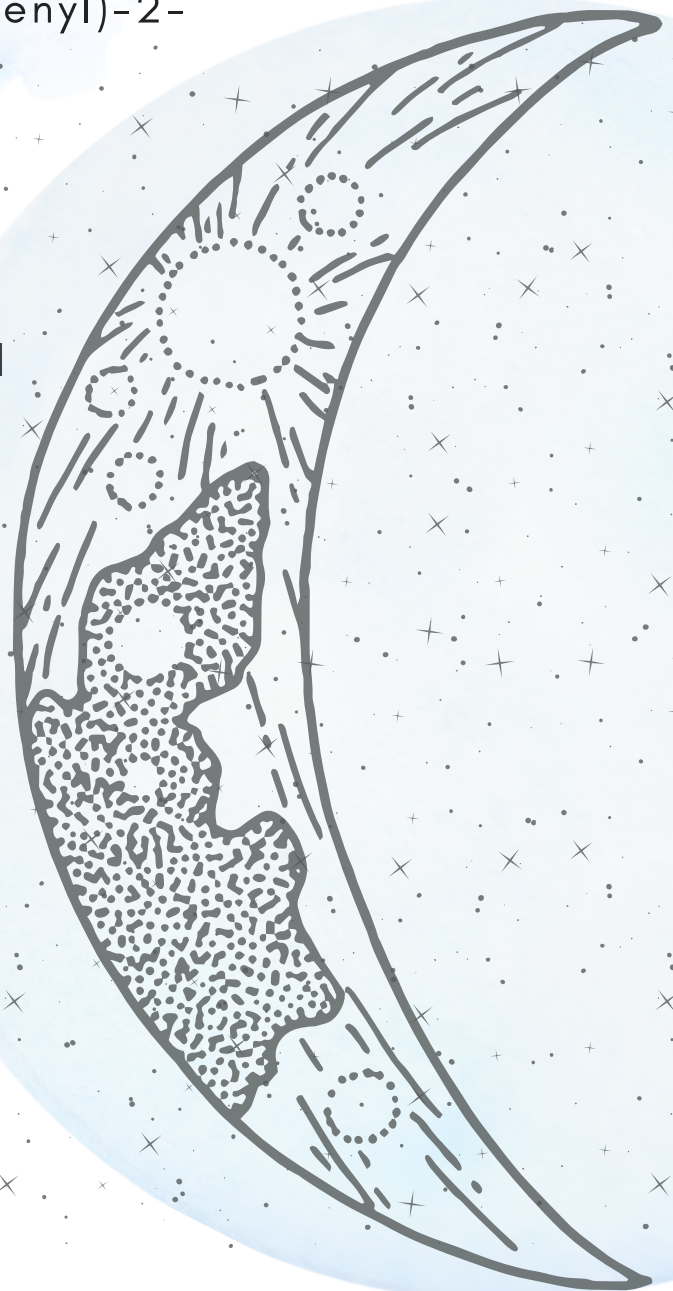
DRUG TYPE: synthetic

LEGAL STATUS: legal with a medical prescription when clinically indicated

CONTROLLED SUBSTANCE (USA):
Schedule III

SPRAVATO (ESKETAMINE)

- Spravato (esketamine)
- FDA approved in 2019, marketed by Janssen
- Nasal spray
- Must be used in conjunction with specific oral antidepressant medications
- Common effects: dissociation, sedation, sleepiness, fainting, dizziness, spinning sensation, anxiety, or feeling disconnected from one's self, thoughts, feelings, space and time



ESKETAMINE

CLINICAL & THERAPEUTICS

APPROVED INDICATIONS

- For adults with treatment-resistant depression
- For depressive symptoms in adults with major depressive disorder with suicidal thoughts or behaviors

TREATMENT DELIVERY

- Requires patient observation and monitoring by a healthcare provider for 2 hours after administration
- Only administered in certified medical offices and clinics that have enrolled in Spravato's program (see [REMS](#))

SAFETY & TOLERABILITY

- Most common adverse reactions of Spravato plus oral antidepressant: dissociation, dizziness, nausea, sedation, vertigo, hypoesthesia, anxiety, lethargy, blood pressure increased, vomiting, feeling drunk, euphoric mood, and vertigo

RECOMMENDED DOSING

- Initial dose: 56 mg
- Induction phase (weeks 1 to 4): 56 mg or 84 mg administered twice per week
- Maintenance phase (weeks 5 to 8): 56 mg or 84 mg administered once weekly administered every 2 weeks or once per week (week 9 and after)
- Maintenance phase (week 9 and after): 56 mg or 84 mg administered once weekly administered every 2 weeks or once per week depending on an individual's response

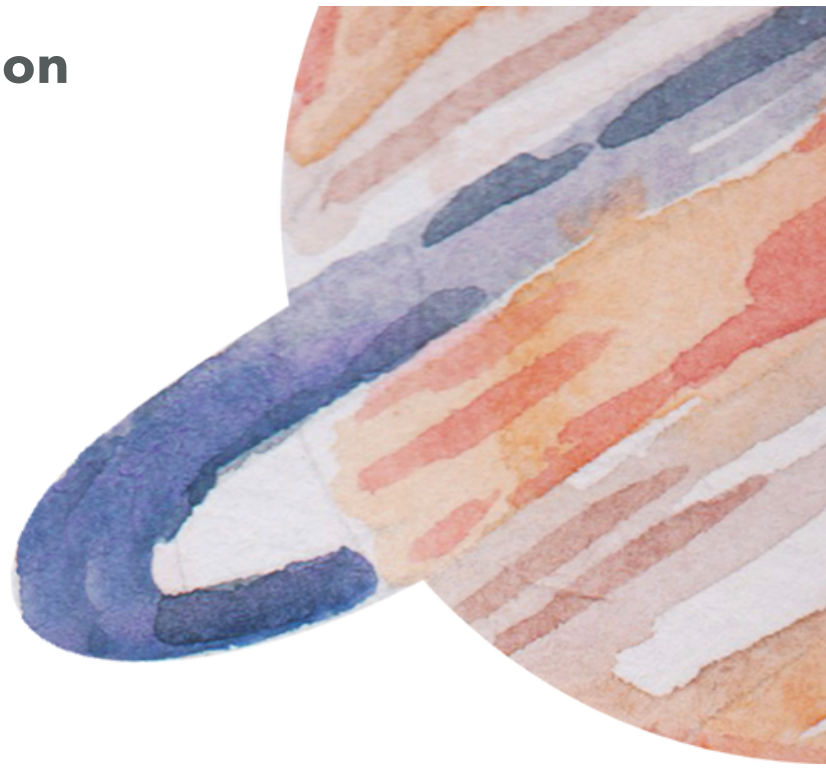
ESKETAMINE CLINICAL TRIAL EXCLUSIONS

- Substance use disorder, active or within the last 6 months
- Current or past psychosis
- Bipolar disorder

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- Understand psychedelic pharmacology, therapeutic techniques, and modern clinical trials



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AYAHUASCA

N,N-DIMETHYLTRYPTAMINE (DMT)

Ayahuasca is a mixture of at least two types of plants, most commonly *Psychotria viridis* and *Banisteriopsis caapi*, that contain N,N-dimethyltryptamine (DMT) and monoamine oxidase inhibitors (MAOI). Originating in the Amazon basin, its use in shamanic ceremonies for spiritual and medicinal purposes dates back centuries. The word "ayahuasca" is Quechua and translates as "the vine or rope of the dead". To this day, many indigenous peoples uphold the tradition in their cultures, and it is also used sacramentally by a number of organized religions. Interest by Western societies has steadily increased over the last few decades because of its purported capacity to heal intractable diseases and exert positive effects on health and wellbeing.

BRAND NAME: none

CHEMICAL NAME: N,N-dimethyltryptamine (DMT) and harmala alkaloids [7-Methoxy-1-methyl-9H-pyrido[3,4-b]indole (harmine); 4,9-Dihydro-7-methoxy-1-methyl-3H-pyrido[3,4-b]indole (harmaline); 1,2,3,4-tetrahydro-harmine (tetrahydroharmine)]

DRUG CLASSIFICATION: psychedelic

DRUG TYPE: plant mixture

LEGAL STATUS: legal in some Central and South American countries; illegal in the USA except for legal religious exemption for specific churches in the USA; decriminalized in many countries

CONTROLLED SUBSTANCE (USA): Schedule I

CLINICAL TRIAL SPONSORS

- Sacred Medicines Public Benefit Corporation
- University investigator-initiated studies



AYAHUASCA

CLINICAL & THERAPEUTICS

The therapeutic potential of ayahuasca in the treatment of mood disorders, posttraumatic stress disorder and substance use disorders, is currently under investigation in a small number of clinical trials and surveys. The first randomized placebo-controlled trial of ayahuasca for treatment-refractory depression demonstrated robust and rapid antidepressant effects from a single dose of ayahuasca when compared to placebo. Another study using data from the Global Drug Survey suggests that the rates of alcoholism were lower in ayahuasca users when compared to people that used LSD or mushrooms.

POSITIVE EFFECTS

- Visual distortions
- Vivid imagery with eyes open or closed
- Purging (physical and emotional)
- Auditory and visual hallucinations
- Feelings of expansiveness
- Feelings of oneness and connection with others and the universe
- Heightened emotions
- Transcendence of space and time
- Ego dissolution
- Mystical and spiritual experiences
- Altered cognition
- Introspection and insightfulness
- Euphoria
- Physical sensations

NEGATIVE EFFECTS

- Panic attacks, anxiety, or confusion
- Nausea or vomiting
- Diarrhea
- Psychological distress
- Physical discomfort
- Impaired concentration and focus, disordered thinking
- Dizziness
- Disorientation
- Muscle weakness or tension
- Muscle spasms
- Light sensitivity
- Pupil dilation
- Body temperature fluctuations
- Dysphoria
- Paranoia
- Delusions
- Seizures (rare)

N,N-DIMETHYLTRYPTAMINE (DMT)

AYAHUASCA

CLINICAL & THERAPEUTICS

INDICATIONS UNDER STUDY FOR AYAHUASCA OR DMT

- Treatment-resistant depression
- Phase 1 healthy individuals (safety trial for DMT)

MECHANISMS OF ACTION

- Harmala alkaloids inhibit MAO in the gut allowing DMT to reach the brain
- Potent partial agonist at serotonin 2A (5-HT_{2A}) receptors, the primary target for subjective effects; agonist at other 5-HT subtypes
- Sigma-1 receptor agonist
- TAAR-1 agonist
- Modulation of glutamatergic system

Ayahuasca induces non-ordinary states of consciousness where a person may experience visionary states, alterations in mood and perceptions, and physical and emotional purging. In traditional lineages, music and singing of special songs called Icaros are predominant features of the ritual, and many who practice with ayahuasca carry and pass down these ways of working with the medicine. The journeyer is supported by these healing songs if physical (vomiting, diarrhea, shaking) and emotional purging comes, or as they transverse their deepest inner worlds. After drinking ayahuasca, it's a common practice for groups to meet the following morning to share and process the experience with others in integration circles. Many keep the diet in place for at least 3-7 days to solidify the effects of the plant medicine and further reflect on the meaning and insights brought into conscious awareness.

Hearing of the potential of ayahuasca to treat mental health conditions, a growing number of individuals are seeking out ayahuasca at retreat centers in Central and South America, church ceremonies, and underground community circles. Before partaking, people usually follow a special diet, called a 'dieta' in traditional practices, to cleanse and prepare the body for upcoming ayahuasca experiences. Typically, gatherings last for a weekend or up to a few weeks, with multiple occasions where ayahuasca is consumed

N,N-DIMETHYLTRYPTAMINE (DMT)

AYAHUASCA

CLINICAL & THERAPEUTICS

Recent neuroscience research suggests the active components of ayahuasca can induce neuroplasticity and the generation of new neurons. Although this has not been demonstrated in human brains, these findings lend support to a neurobiological underpinning for the changes in thought patterns and behaviors ayahuasca drinkers report. This isn't to say the psychospiritual aspects of the experience aren't necessary or important, but describes how neural pathways may adapt to allow for new ways of seeing and being in the world.

Pharmaceutical sponsors are interested in taking ayahuasca through the FDA development path with hopeful approval. Developing botanical drugs is challenging, only two have ever become FDA-approved, and many who use ayahuasca as a sacrament question its place in modern medical practices, particularly if profit motives are predominant. 'Pharmahuasca' refers to a synthetic mixture of DMT and harmala alkaloids.

THERAPEUTIC APPROACH

- Supportive therapy and integration sessions
- Group administrations (planned)

DOSING OF DMT IN CLINICAL TRIALS

- 54 mg, 69 mg, 90 mg, 115 mg (IV)

DOSING OF AYAHUASCA IN CLINICAL TRIALS

- 0.36 mg/kg DMT (Palhano-Fontes, 2017)
- Duration of effects: 4 hours

SAFETY & TOLERABILITY

- Non-toxic
- Drug interactions can be serious
- Severe psychological distress or psychotic breaks can occur

While not identical in effects to the plant-based brews, a synthetic version is available and could be a drug studied for medical use. DMT administrations through routes other than oral ingestion are another method underdevelopment and could be regulated as medicines. To mimic ayahuasca, a new trial will examine slow IV administrations of DMT to prolong the effects and maintain steady levels of DMT in the blood. Otherwise, the duration of effects is only about 15 minutes for smoked or single injections of DMT.

N,N-DIMETHYLTRYPTAMINE (DMT)

AYAHUASCA

NON-MEDICAL USES

Indigenous peoples of the Amazon discovered ayahuasca and passed down the sacred knowledge of these practices for many generations. Only in the 1950s did a few Westerners really catch on to the healing properties and take interest in partaking in ayahuasca ceremonies. Since then there has been a boom of 'ayahuasca tourism' where people from all over the globe are trekking to retreat centers in Central and South America. The plants are exported out of the jungles of the Amazon to be served at underground gatherings across the world. This blossoming interest and resulting over harvesting of ayahuasca threatens the sustainability of the plants and the cultures who hold plant medicines as central tenants in their cosmologies. Conservation of the plants and their natural ecosystems, and reciprocity to the indigenous peoples who shared their long-held wisdom of the plants, must be paramount as psychedelics come into the focus of mainstream global culture.

COMMON STREET NAMES

- Huasca
- Yajé
- Caapi
- Daime
- Vegetal
- Grandmother plant
- Spirit molecule

ROUTES OF ADMINISTRATION

- Oral (plant brew)
- Oral (freeze dried capsules of plants)
- Smoked (DMT)
- Intravenous (DMT)
- Intramuscular (DMT)

POPULAR SETTINGS

- Malocas
- Yurts
- Ceremonies and rituals
- Natural environments
- Living rooms

COMMON PREPARATIONS

- *Banisteriopsis caapi*
- *Psychotria viridis*
- Over 100 other plants documented

N,N-DIMETHYLTRYPTAMINE (DMT)

AYAHUASCA

NON-MEDICAL USES

AYAHUASCA DOSES*

Analysis of ayahuasca from several sources by Callaway:

- DMT concentration: between 0.16 mg/mL and 14.15 mg/mL (although some samples did not contain any DMT)
- THH concentration: between 0.49 mg/mL and 23.80 mg/mL
- Harmaline concentration: between 0.01 mg/mL and 0.9 mg/mL
- Harmine concentration: between 0.45 mg/mL and 22.85 mg/mL
- Doses vary across traditions between 20-200 mL

*Potency varies across brews made from various plants

PRIMARY RISKS

- Other plants added to the mixture
- Complications with pre-existing health conditions
- Drug interactions with contraindicated medications
- Sexual assaults
- Vulnerable states; misjudgements
- Psychological distress

FACTORS AFFECTING RISK PROFILE

- Dose
- Drug/medication interactions
- Pre-existing health conditions
- Set and setting



N,N-DIMETHYLTRYPTAMINE (DMT)

5 - M e O - D M T

5-METHOXY-N,N-DIMETHYLTRYPTAMINE

A tryptamine derivative, 5-MeO-DMT is a very strong, fast-acting psychedelic compound with a short duration. The effects include vision and auditory alterations, out-of-body experiences and mystical type experiences, but unlike other classical psychedelics the visionary effect is often eclipsed by the emotional impact of the experience. 5-MeO-DMT has a different chemical structure and effect profile from N,N-DMT (compound in ayahuasca), and is considered more intense and powerful.

BRAND NAME: none

CHEMICAL NAME: 5-methoxy-N,N-dimethyltryptamine

DRUG CLASSIFICATION:

empathogen/entactogen

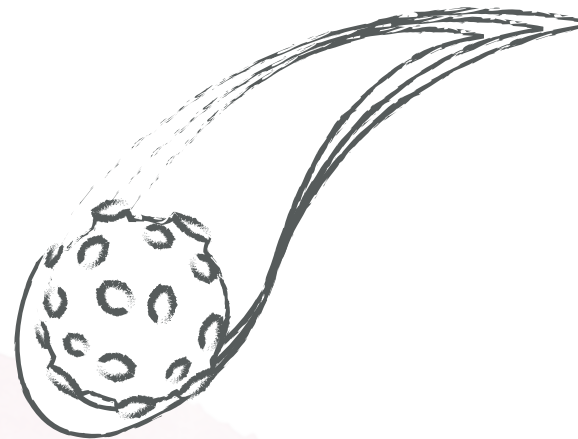
DRUG TYPE: classical psychedelic

LEGAL STATUS: illegal the US; other countries it is unscheduled and unregulated (i.e. Mexico)

CONTROLLED SUBSTANCE (USA):
Schedule I

CLINICAL TRIAL SPONSORS

- GH Research Limited
- Beckley PsyTech
- Usona Institute



5 - M e O - D M T

CLINICAL & THERAPEUTICS

5-MeO-DMT can be extracted from specific plant species or from the venom of the *Incilius alvarius* toad (aka, *Bufo alvarius*, Sonoran Desert or Colorado River toad). The bufotoxin venom contains 5-MeO-DMT and bufotenine, both psychoactive substances. A full dose (50 mg) of vaporized bufotoxin consists of approximately 10-15% of 5-MeO-DMT and induces mystical type-experiences of similar intensity to high-dose psilocybin (30 mg/70 kg). The duration of effects depends on the route of administration but for smoked 5-MeO-DMT effects are typically felt 0-30 seconds after ingestion, peak around 15 minutes, and dissipate 30 minutes after administration.

POSITIVE EFFECTS

- Euphoria
- Changes in bodily sensations
- Out of body experiences
- Increased or decreased visual acuity
- Unity and interconnectedness
- Perception of infinity
- Time distortion
- Catharsis
- Ego dissolution
- Bliss
- Spiritual experiences
- Auditory distortions or hallucinations

INDICATIONS UNDER STUDY FOR 5-MeO-DMT

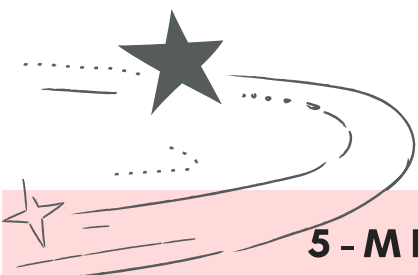
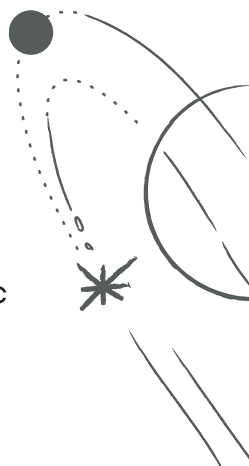
- Treatment-resistant depression

NEGATIVE EFFECTS

- Nausea or vomiting
- Anxiety
- Confusion, delusion
- Pupil dilation
- Loss of motor control, spastic movements
- Tremors, muscle spasms
- Respiratory depression
- Skin flushing
- Disorientation
- Temperature regulation suppression

MECHANISMS OF ACTION

- Non-selective agonist at serotonin receptors (5-HT_{2A}, 5-HT_{2C}, 5-HT_{1A})
- Bufotenine (metabolite of 5-MeO-DMT and often co-occurring compound in plants and toad) - high affinity 5-HT_{2A} receptor agonist
- Acts at many glutamate, dopamine, and acetylcholine receptors



5 - M e O - D M T

CLINICAL & THERAPEUTICS

THERAPEUTIC APPROACH (MAPS)

- Supportive therapy and integration care
- New clinical approaches under development

LABORATORY DOSING

- Duration of effects 15 to 90 minutes
- Inhalation (~6 to 12 mg)
- IV (~0.7 to 3.1 mg)
- Sublingual or intranasal (~10 mg)

SAFETY & TOLERABILITY

- Data from controlled clinical trials unavailable
- Low potential for dependence in medical and non-medical settings

Some suspect 5-MeO-DMT containing toad venom was used by ancient civilizations in shamanic healing ceremonies, but conclusive evidence is lacking. Dating back to the late 8th century, some snuffs of South American indigenous tribes were found to contain 5-MeO-DMT. It was first synthesized in 1936, only to become known to a small number of people in the 1970s. Its expanding popularity over the decades, and its commercial distribution through mail orders, prompted its placement on the Schedule I list of controlled substances in 2011.

5-MeO-DMT can be easily synthesized in a laboratory, as demonstrated here by Hamilton Morris. While some advocates argue that the constituents of bufotoxin might have synergistic effects, the threat of over harvesting venom from toads and the impact on local communities in the Sonoran Desert is a growing concern. Synthetic 5-MeO-DMT is an alternative that can alleviate the peril of the toads and their natural habitats. Synthetic drugs allow for much more precise dosing which is paramount for a drug as potent as 5-MeO-DMT. Drug development sponsors are now making a synthetic version to test for treating mental health conditions after anecdotal reports of 5-MeO-DMT bringing relief for depression, anxiety, substance use, and mood disorders.

5 - M e O - D M T

NON-MEDICAL USES

COMMON STREET NAMES

- 5-MeO
- Toad medicine
- Sonoran toad
- Colorado river toad venom
- Bufo
- God molecule
- Yopo

POPULAR SETTINGS

- Home
- Natural environments
- Ceremonies
- Therapeutic settings

ROUTES OF ADMINISTRATION

- Inhalation (smoked)*
- IV
- Sublingual
- Intranasal (snorted)
- Rectal

SMOKED TOAD VENOM DOSAGE (AT LEAST 10% IS 5-MEO-DMT)

- Threshold 10-20 mg
- Moderate 20-50 mg
- Common 50-70 mg
- Strong 70-100 mg

COMMON APPEARANCES

- Dried toad venom (tan crystals)

*Synthetic and toad forms differ in terms of dosing and route of administration. Toad venom can only be administered through vaporization because of other chemicals present in the venom.

PRIMARY RISKS

- Unknown or imprecise dosing can lead to acute and prolonged adverse effects
- Complications with pre-existing health conditions
- Unskilled guides and facilitators
- Psychological distress/spiritual emergency

FACTORS AFFECTING RISK PROFILE

- Dose
- Pre-existing health conditions
- Set and setting
- Psychological preparation



LSD

LYSERGIC ACID DIETHYLAMIDE

One of the most well known classical psychedelics, lysergic acid diethylamide aka LSD, came into this world through an accidental discovery by the chemist Albert Hoffman on April 19, 1943. He first made LSD-25 in 1938 but didn't become aware of the mind-shifting properties until he unknowingly absorbed a dose in the laboratory and felt the full effects in a harrowing bicycle ride home. The profound trip led to a quest by his employer Sandoz Laboratories to find out how this substance could be used in clinical applications. They distributed LSD to doctors and therapists around the world to administer to their patients and themselves in hopes of finding a medical use.

BRAND NAME: Delysid (1950-60s)

CHEMICAL NAME: lysergic acid diethylamide

DRUG CLASSIFICATION: classical psychedelic

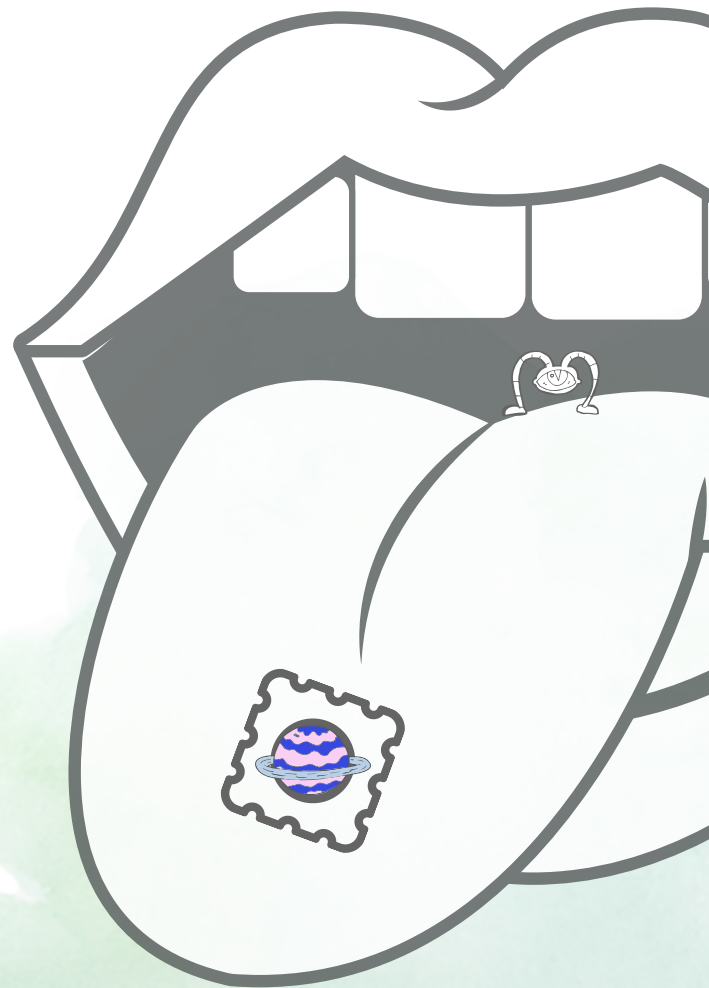
DRUG TYPE: synthetic

LEGAL STATUS: illegal

CONTROLLED SUBSTANCE (USA): Schedule I

CLINICAL TRIAL SPONSORS

- [Mind Medicine](#)
- [MAPS](#)
- [Beckley Foundation](#)
- Investigator-initiated studies



LSD

CLINICAL & THERAPEUTICS

The research lasted for a few decades and amassed reports of therapeutic value for a wide range of mental health conditions. But by the mid-1960s, the drug had gained popularity outside of clinical settings and became associated with the counterculture, anti-war agenda, and hippie movement. In 1970, the Controlled Substance Act was passed into law, placing LSD and other psychedelics in the most restrictive class - Substance I Controlled Substances. LSD research was shut down and the possession and use of LSD was criminalized with the highest penalties for offenders.

POSITIVE EFFECTS

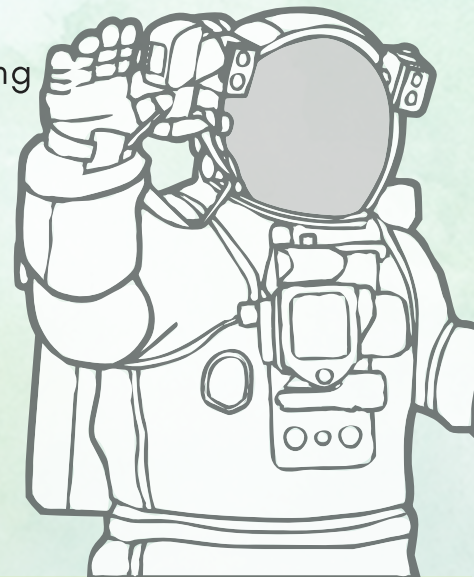
- Visual distortions
- Vivid imagery with eyes open or closed
- Auditory and visual hallucinations
- Sensory synesthesia
- Feelings of expansiveness
- Feelings of oneness and connection with others and the universe
- Heightened emotions
- Transcendence of space and time
- Ego dissolution
- Mystical experiences
- Altered cognition
- Introspection and insightfulness

INDICATIONS UNDER STUDY FOR LSD

- Pain management
- ADHD
- Anxiety related to a life-threatening illness

NEGATIVE EFFECTS

- Panic attacks, anxiety, or confusion
- Paranoia
- Dysphoria
- Irrational and reckless behavior
- Impaired concentration and focus, disordered thinking
- Dizziness
- Disorientation
- Restlessness
- Weakness
- Numbness
- Nausea or vomiting
- Light sensitivity
- Pupil dilation
- Flashbacks
- Tremors
- Perspiration



LYSERGIC ACID DIETHYLAMIDE

LSD

CLINICAL & THERAPEUTICS

MECHANISMS

OF ACTION

- High-affinity agonist at serotonin 2A (5-HT_{2A}) receptor, the primary target for subjective effects
- Agonist at most serotonin receptors subtypes 5-HT_{1A}, 5-HT_{2B}, 5-HT_{2C}, 5-HT_{5A}, 5-HT₆; agonist at dopamine (D₂) receptors
- Modulation of serotonergic, dopaminergic, and glutamatergic systems

THERAPEUTIC APPROACH

- Microdose protocols (very low dose repeated every few days)
- LSD-assisted psychotherapy

THERAPEUTIC DOSING

- Oral
- Very low doses: 5, 10, 20 µg
- Typical dose: 100 µg
- Medium dose: 200 µg
- Duration of effects 6 to 12 hours

LSD is a potent substance for altering consciousness. The dosage is in micrograms (µg) - a tiny amount compared to most other drugs - and the duration of effects is long (anywhere from 6 to 12 hours). Now over 50 years since it was banned, LSD is once again under study in clinical trials. The first publication of modern-era LSD research reported significant benefits for people coping with anxiety associated with life-threatening illnesses. Other studies are interested in how LSD microdosing (tiny sub-perceptual, repeated doses) can affect pain severity or ADHD symptoms.

Research came to a screeching halt, but LSD did not disappear - it went underground. According to a 2017 report, an estimated 10% of individuals in the US have used LSD in the past and 0.7% had taken it in the last year (drugabuse.org). From 2015 to 2018, LSD consumption by US adults increased 56.4%.

SAFETY & TOLERABILITY

- Well tolerated in individuals screened for specific physiological and psychological health criteria
- Low potential for dependence in medical and non-medical settings
- Common adverse reactions in a trial: illusion, anxiety, emotional distress, feeling abnormal, feeling cold

LYSERGIC ACID DIETHYLAMIDE

LSD

NON-MEDICAL USES

COMMON STREET NAMES

- Acid
- L
- Cid
- Lucy
- Dots
- Mellow yellow
- Window pane
- Blotter
- Orange sunshine

POPULAR SETTINGS

- Home
- Natural environments
- Electronic music festivals
- House parties
- Concerts
- Art festivals
- Therapeutic settings

ROUTES OF ADMINISTRATION

- Oral
- Subcutaneous

COMMON APPEARANCES

- Liquid drops
- Blotter paper
- Tablets (microdots) or capsules
- Candy
- Patch (for skin)

As with all psychedelics, the environment and person's psychological state can dramatically impact the LSD experience. Not everyone is a suitable candidate for taking LSD, particularly those with a background or family history of psychotic disorders (schizophrenia, bipolar disorder, etc). Caution and harm reduction practices are essential for safe use.

LSD DOSES

- Microdose: 5 - 19 μg
- Low dose: 20 - 75 μg
- Moderate dose: 76 - 200 μg
- High dose: 201 - 400 μg
- Very high dose: >400 μg

PRIMARY RISKS

- Physical harms caused by changes in judgement and dangerous behaviors
- Complications with pre-existing health conditions
- Flashbacks

FACTORS AFFECTING RISK PROFILE

- Dose
- Pre-existing health conditions
- Set and setting

CANNABIS

$\Delta 9$ -TETRAHYDROCANNABINOL (THC), CANNABIDIOL (CBD)

Cannabis is a flowering herb in the plant family Cannabaceae. The plant has been used for medicinal and industrial purposes for thousands of years by many cultures across the globe. It contains at least 113 naturally occurring chemical compounds called cannabinoids. Some cannabis varieties contain a psychoactive cannabinoid called tetrahydrocannabinol (THC) that induces a range of subjective effects dependent on the dose. Another cannabinoid named cannabidiol (CBD) does not cause intoxication but is used for health benefits. The flowers of *Cannabis sativa* and *Cannabis indica* are smoked, vaporized, eaten, or topically applied for recreational and medicinal purposes. Cannabis plants cultivated for industrial (no THC, non-drug) use are referred to as hemp and have many uses when processed for textiles, paper, health foods, building materials, and biodegradable plastics.

BRAND NAME: Epidiolex (cannabidiol), Marinol (dronabinol), Syndros (dronabinol), and Cesamet (nabilone)

CHEMICAL NAME: $\Delta 9$ -tetrahydrocannabinol (THC), cannabidiol (CBD)

DRUG CLASSIFICATION: endocannabinoids

DRUG TYPE: THC/CBD (synthetic), cannabis plants

LEGAL STATUS: mixed in US (legal with prescription, legal in some US states, decriminalized in some states, US federally illegal); varies world-wide

CONTROLLED SUBSTANCE (USA): Schedule I (THC/CBD/cannabis plants)

CLINICAL TRIAL SPONSORS

- Pharmaceutical companies
- University investigator-initiated studies



CANNABIS

CLINICAL & THERAPEUTICS

According to the United States federal government, cannabis remains illegal as Schedule I Controlled Substance. However, at least 18 states and the District of Columbia have fully legalized cannabis use and the majority of the other states have either legalized medical cannabis use and/or decriminalized personal use.

The FDA has not approved cannabis for the treatment of any health conditions but has approved Epidiolex (cannabidiol), a cannabis-derived drug product, and three synthetic cannabis-related drug products - Marinol (dronabinol), Syndros (dronabinol), and Cesamet (nabilone). The proclaimed therapeutic effects of cannabis span many conditions but the largest amount of evidence from research supports the benefits of cannabis for pain reduction, nausea and vomiting induced by chemotherapy, and muscle spasticity in multiple sclerosis.

POSITIVE EFFECTS

- Changes in sensory perceptions
- Elevated mood
- Alterations in sense of time
- Relaxation
- Euphoria
- Increase in sociability
- Heightened creativity

COMMON INDICATIONS FOR MEDICAL CANNABIS

- Pain
- Posttraumatic stress disorder
- Epilepsy
- Cancer and symptoms related to treatments
- Neurodegenerative diseases

NEGATIVE EFFECTS

- Paranoia, anxiety, panic, and psychosis
- Dry mouth
- Disorientation
- Delusions and hallucinations (high doses)
- Increased heart rate
- Difficulty thinking clearly
- Altered judgement
- Loss of coordination

NEGATIVE EFFECTS OF PROLONGED USE

- Brain fog
- Breathing problems
- Dependence
- Impaired memory, concentration, and problem-solving
- Fertility issues

CANNABIS

CLINICAL & THERAPEUTICS

Although not backed by substantial scientific evidence, people self-medicate with cannabis and CBD to reduce anxiety and depression symptoms, improve sleep quality, manage stress, and mitigate PTSD symptoms. However, some research has found that heavy use of high-potency cannabis can be associated with adverse mental health consequences, increased risk for worsening of psychiatric symptoms and substance use disorders, and impaired learning and memory.

MECHANISMS OF ACTION

- THC: activation of cannabinoid CB1 receptors
- CBD: antagonist of GPR55 receptors; inverse agonist of GPR3, GPR6, and GPR12; allosteric modulator of opioid receptors; PPAR γ agonism; inhibition of voltage-gated cation channels; intracellular calcium release

BRAND NAME (GENERIC) / PHARMACEUTICAL COMPANY

Cannabis-derived drug

- Epidiolex (cannabidiol) / GW Pharmaceuticals

Synthetic cannabis-related drugs

- Marinol and Syndros (dronabinol) / Solvay Pharmaceuticals, PAR Pharmaceutical Companies, Alkem Labs
- Cesamet (nabilone) / Eli Lilly and Company, Valeant Pharmaceuticals

PREPARATIONS AND APPROACHES

- Whole plant preparations
- Edibles
- Tinctures
- Topicals
- Cannabis-assisted psychotherapy

CANNABIS DISPENSARIES

- Located in states permitting medical or recreational cannabis
- Doctor issued medical cannabis license required in some states
- Carry a variety of cannabis flowers, tinctures (oils), edibles, topicals, and cannabis-related merchandize
- Bud tenders or medical consultation available for advice on cannabis products.

CANNABIS

CLINICAL & THERAPEUTICS

DOSING

- Dosing and frequency of administration varies widely. Duration of effects depends on the route of administration.

SAFETY & TOLERABILITY

- Low physiological toxicity, no lethal overdoses
- Well tolerated in individuals without pre-existing psychotic disorders
- Challenging psychological experiences can occur
- Adverse effects associated with duration and amount of use

Cannabis-assisted psychotherapy is an approach where a person consumes cannabis with the intention of exploring emotions, thoughts and sensations under the guidance of a therapist. Under the relaxing effects of cannabis, a person may more easily approach and work with difficult emotions from a different self view point. This technique is relatively novel and encompasses other therapeutic practices such as breathing and relaxation exercises. Cannabis-assisted psychotherapy is only available in states where cannabis is legal.



Δ9-TETRAHYDROCANNABINOL (THC), CANNABIDIOL (CBD)

CANNABIS

NON-MEDICAL USES

COMMON STREET NAMES

- Cannabis
- Marijuana
- Weed
- Herb
- THC
- CBD

POPULAR SETTINGS

- Home
- Outdoor environments
- Spiritual practices
- Hikes
- House parties
- Electronic music festivals

ROUTES OF ADMINISTRATION

- Inhaled (smoked)
 - Joints
 - Pipes
 - Bongs
 - Blunts
- Inhaled (vaporized)
- Oral
 - Edibles
 - Drinks
 - Capsules
 - Tinctures (oils)

DOSING

Dosing and frequency of administration varies widely. Duration of effects depends on the route of administration.

PRIMARY RISKS

- Anxiety, panic attacks, or paranoia
- Memory and problem-solving impairment
- Misuse, dependence, and addiction
- Increased risk of psychosis or worsening of schizophrenia symptoms in those at high genetic risk

FACTORS AFFECTING RISK PROFILE

- Pre-existing health conditions
- Dosage
- Environment
- Duration of use

IBOGAINE

12-METHOXYIBOGAMINE

Iboga refers to perennial rainforest shrubs in the Apocynaceae family, including the most well known species *Tabernanthe iboga*. Customarily used in shamanic healing and initiation ceremonies of Central African traditions, iboga is a plant with roots and bark containing the psychoactive alkaloid ibogaine. People of Gabon have practiced with iboga as a sacrament in their Bwiti religion for hundreds of years. Through passed down knowledge accumulated over thousands of years, providers of iboga are extensively trained to work with this plant medicine in West African traditions.

BRAND NAME: none

CHEMICAL NAME: 12-methoxyibogamine

DRUG CLASSIFICATION: plant mixture

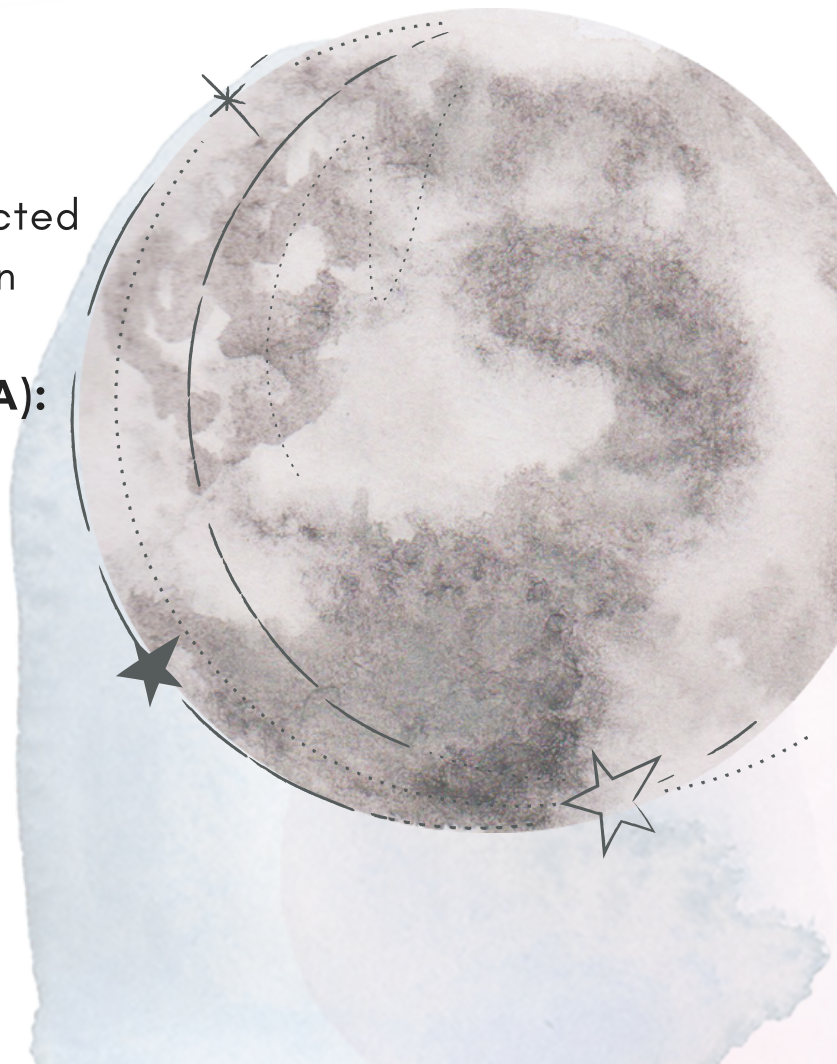
DRUG TYPE: plant derived

LEGAL STATUS: illegal or restricted in most countries; unscheduled in Mexico and West Africa

CONTROLLED SUBSTANCE (USA): Schedule I

CLINICAL TRIAL SPONSORS

- University investigator-initiated studies
- MAPS
- Sacred Medicines Public Benefit Corporation
- New pharmaceutical companies



IBOGAINE

CLINICAL & THERAPEUTICS

Ibogaïne became known as a helpful tool for reducing opioid withdrawal and craving in 1962 after Howard Lotsof accidentally discovered the anti-addictive effects after ingesting ibogaïne. It has also been shown to reverse addiction to stimulants, alcohol, and nicotine. Preclinical research and phase 1 clinical studies were conducted in the early 1990s to evaluate the safety of ibogaïne, but the studies were ended due to intellectual property disputes and a death associated with ibogaïne outside of medical contexts. Currently, it is not approved for the treatment of addiction or any other medical conditions.

POSITIVE EFFECTS (HIGHER DOSES)

- Dream-like state
- Vivid imagery with eyes closed
- Hallucinations and visual distortions
- Memory recall
- Introspection
- Conceptual thinking

POSITIVE EFFECTS (LOWER DOSES)

- Increased energy
- Stimulant effects
- Lack of appetite

NEGATIVE EFFECTS

- Loss of coordination
- Nausea
- Vomiting
- Sensitivity to light and sounds
- Pupil dilation
- Dizziness
- Tremors
- Anxiety
- Delusions
- Mania or psychosis
- Dehydration/loss of electrolytes
- Seizures*
- Irregular heartbeat
- Increased blood pressure
- Cardiac arrest
- Death from acute heart failure or cardiopulmonary arrest

*Related to acute alcohol or benzodiazepine withdrawal

IBOGAINE

CLINICAL & THERAPEUTICS

Observational studies and case reports show ibogaine can reduce drug craving and withdrawal symptoms, and some individuals had sustained reductions of opioid use 12 months after undergoing ibogaine treatment. Research in animal models report ibogaine to reduce consumption of alcohol, stimulants, and opioids.

INDICATIONS UNDER STUDY FOR IBOGAINE

- Alcohol use disorders
- Methadone detoxification
- Opioid use disorders
- TBI

MECHANISMS OF ACTION

- Potent serotonin reuptake inhibitor
- K-opioid receptor agonist
- μ -opioid receptor agonist and partial agonist (weak)
- Sigma-2 receptor agonist
- Inhibits nicotinic acetylcholine receptors and NMDA receptors
- Modulates many other neurotransmitter systems

Ibogaine clinics operate in Mexico because people can use and possess ibogaine but it is still illegal to use it as a medicine because it is not scheduled or regulated. Ibogaine is illegal or restricted in many countries including the USA (Schedule I substance). With the resurgence in psychedelic research, there is renewed interest in controlled evaluation of ibogaine. A phase 2 trial in Brazil is investigating ibogaine for the treatment of alcohol use disorders; a phase 2 trial in Spain is testing ibogaine for methadone detoxification. Other companies have announced plans to conduct ibogaine research for opioid use disorders.

IBOGAINE

CLINICAL & THERAPEUTICS

THERAPEUTIC APPROACHES

- Ibogaine administration under medical supervision
- Integration and recovery support

THERAPEUTIC DOSING OF IBOGAINE HCL

- 100 mg
- Ascending doses (100 to 600 mg)
- 240 mg
- 240 mg, 320 mg
- 240 mg, 320 mg, 400 mg

SAFETY & TOLERABILITY

- Individuals must be screened for cardiovascular conditions and other pre-existing health conditions
- Contraindicated medications and drugs must be discontinued
- Low potential for dependence in medical and non-medical settings
- Trials ongoing - tolerability data unavailable

The ibogaine experience typically progresses through a visionary phase (4 to 8 hours), an introspection phase (8 to 20 hours), and finally a stimulatory phase (24 to 72 hours).

Unlike most psychedelic substances, ibogaine is associated with serious adverse effects, and even death. Fatalities are usually attributed to other factors such as pre-existing medical conditions, mostly related to cardiovascular dysfunction, and contraindicated medications or drugs.

For these reasons, medical screening (ECG/EKG, liver panel, review of medical conditions) and discontinuation of contraindicated drugs prior to taking ibogaine is extremely important. Ibogaine should never be taken alone; administrations should be under medical supervision with an automated external defibrillator (AED) onsite.

IBOGAINE

NON-MEDICAL USES

Synthetic ibogaine is not widely available because the process to make it is difficult and has yet to be optimized. Iboga plants are grown to source ibogaine. As interest in this plant medicine grows, people must be conscientious of the impacts on the indigenous people who traditionally use iboga and the sustainability of the plants.

COMMON STREET NAMES

- Iboga
- Ibogaine
- Eboga
- Endabuse
- *Tabernanthe iboga*

POPULAR SETTINGS

- Ceremonies
- Initiation rites (Bwiti, Central African traditions)
- Clinics

ROUTES OF ADMINISTRATION

- Oral
- Iboga root (chewed)
- Ibogaine (extracted alkaloid)

DOSES (ORAL) FOR IBOGAINE HYDROCHLORIDE

- 2-3 mg/kg (test dose to check for allergic reaction)
- 6-20 mg/kg (single 'flood dose')
- 1-5 mg/kg (booster dose)
- Dosing should never exceed 24 mg/kg in 24 hours
- 25 mg (Microdosing)

DOSES (ORAL) IBOGA ROOT BARK

- 5-100 grams

FACTORS AFFECTING RISK PROFILE

- Dose (>12 mg/kg increase risk for cardiac abnormalities)
- Pre-existing health conditions
- Contraindicated drugs and medications (including opioid drugs)
- Set and setting

COMMON APPEARANCE

- Iboga root
- Brown powder in capsules

PRIMARY RISKS

- Severe adverse effects or death from underlying cardiac conditions
- Complications with pre-existing health conditions
- Interactions with other drugs or medications
- Psychological distress



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