

# Psychedelics



WITH DALTON

Gisel Murillo

## [COMPANY VISION]

"To make the impossible possible. Dalton Pharma Services uses its scientific and pharmaceutical expertise to bring customer ideas to life. We develop their new drug products, optimize the synthesis of therapeutic candidates, and manufacture them at the highest level of quality."

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# What are Psychedelics?

## Psychedelics

- Psychedelics are a subset of hallucinogenic drugs that alter mood, cognitive processes, and consciousness by influencing how neurotransmitters operate at the synapses of the central nervous system. The consumption of certain psychedelics may produce unpleasant, frightening, or pleasant visual and auditory hallucinations. [1]
- Some of the most well-known psychedelic drugs include LSD, peyote, psilocybin, and DMT.
- Psychedelics are controlled substances around various regulatory agencies due to their high potential for abuse. However, research has shown that psychedelics may play a role in treatments for psychiatric disorders. [1]
- Psilocybin is currently undergoing clinical studies for its potential to treat various conditions such as anxiety, depression, obsessive-compulsive disorder, and problematic drug use. However, there are currently no approved therapeutic products containing psilocybin in Canada or the US. [2, 3]

## Did You Know? [4, 5]

10-20 years

Mental illness can cut 10 to 20 years from a person's life expectancy

Mental illness affects people of all ages, education, income levels, and cultures



264 million

Depression affects 264 million people worldwide

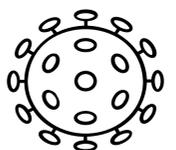
Mental health will indirectly affect all Canadians, and 1 in 5 people in Canada will personally experience a mental health problem



284 million

Anxiety affects 284 million people worldwide

The current and ongoing financial impacts of COVID-19 have negatively impacted people's mental health



75%

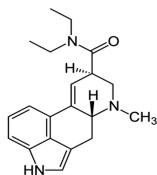
75% of children with mental health problems do not have access to specialized treatment services

# Types of Psychedelics

Psychedelic hallucinogens are classified by their primary mode of action.

## Classical Psychedelics [6, 7]

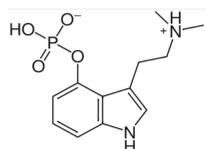
Classical psychedelics exert their effects primarily by an agonist (or partial agonist) action on brain serotonin 5-hydroxytryptamine (5-HT) 2A receptors. [8] Classical psychedelics include:



LSD

(Lysergic acid diethylamide)

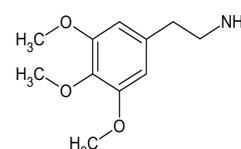
- Found in a fungus that grows on rye and other grains
- Hallucinogenic, synthetic substance, can cause bad trips



Psilocybin

[3-(2-Dimethylaminoethyl)-1H-indol-4-yl] dihydrogen phosphate

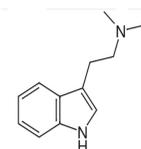
- Naturally occurring psychedelic prodrug found in "magic mushrooms," hallucinogenic, can cause bad trips



Mescaline

(3,4,5- trimethoxyphenylathylamine)

- Found in small spineless cactus, mescaline is the active ingredient in peyote



DMT

(N, N-dimethyltryptamine)

- Hallucinogenic chemical compound found in many plants and animals

## Other Psychedelics [6, 7]

A few other drugs that produce psychedelic effects but have a different mechanism of action are entactogens and dissociative or psychedelic anesthetics.

Entactogens – exert their effects primarily by an antagonist action on the N-methyl-D-aspartate (NMDA) subtype of the glutamate receptor. [1, 9] Entactogens include:

- 3,4-Methylenedioxymethamphetamine or MDMA
  - Also known as “ecstasy” or “molly,” addictive, harmful short-and-long-term mental and physical effects

Dissociative or psychedelic anesthetics include:

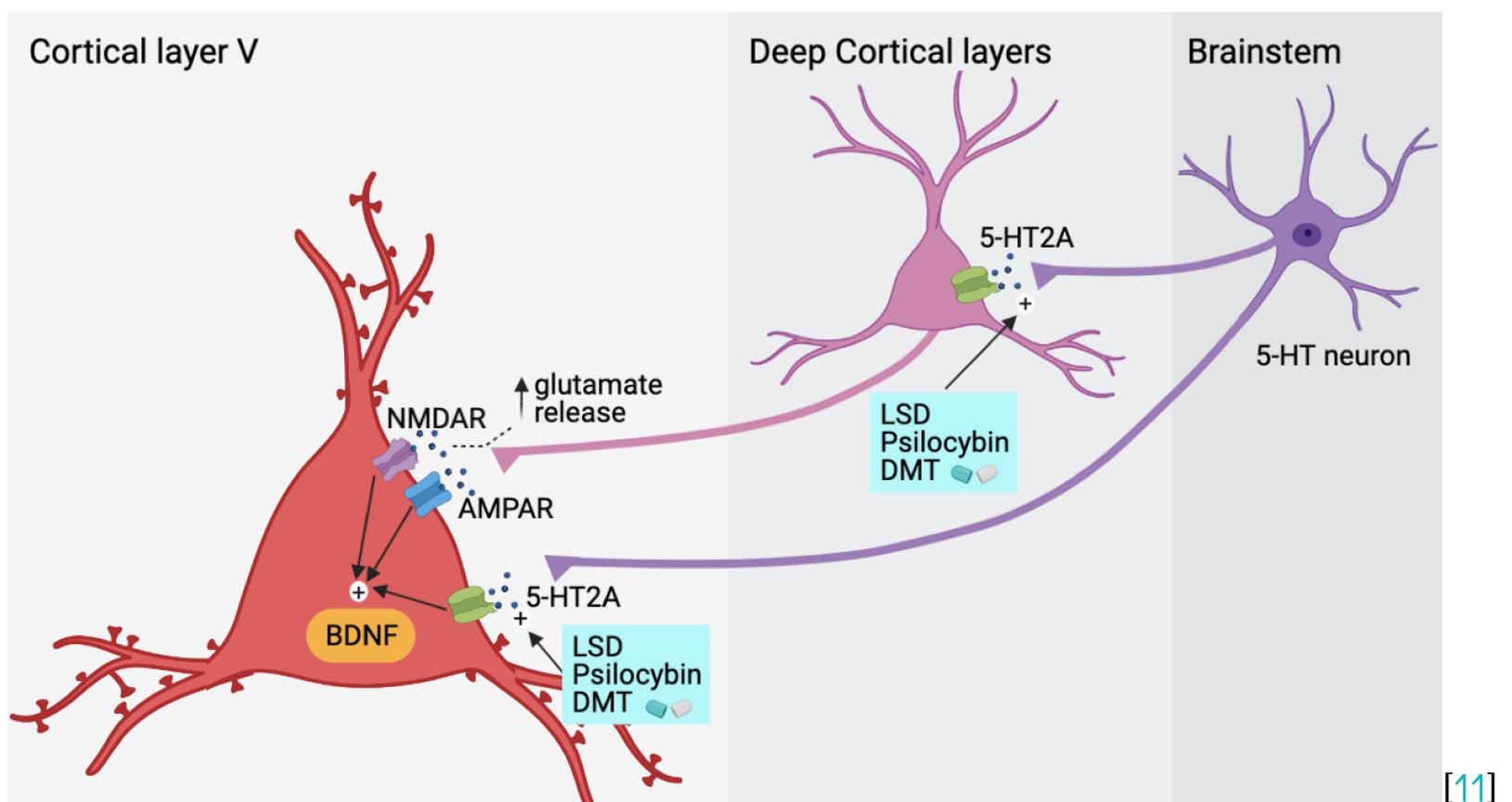
- Ketamine
  - Causes detachment from reality, may lead to risk-taking behaviours, sometimes used as a “date rape” drug, surgery anesthetic for humans and animals
- PCP Phencyclidine
  - Also known as “angel dust,” causes detachment from reality, may lead to risk-taking behaviours, surgery anesthetic no longer used due to serious side effects

\* bad trips = non-ordinary states of consciousness

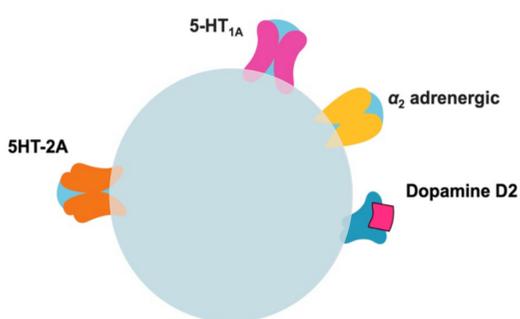
# Mechanism of Action

## Mechanism of Action Overview

- Psychedelics are agonists or partial agonists at brain serotonin receptors, meaning they activate serotonin upon binding.
- Psychedelics predominantly target 5-hydroxytryptamine 2A (5-HT<sub>2A</sub> receptors). 5-HT<sub>2A</sub> is an excitatory postsynaptic receptor and a subfamily of 5-HT receptors that bind the endogenous neurotransmitter serotonin.
- Psychedelics particularly target 5-HT<sub>2A</sub> expressed on apical dendrites of neocortical pyramidal cells in layer V. [1] This triggers a dramatic increase in the release of the excitatory neurotransmitter glutamate in the cortical, thalamic, and limbic regions. [10]

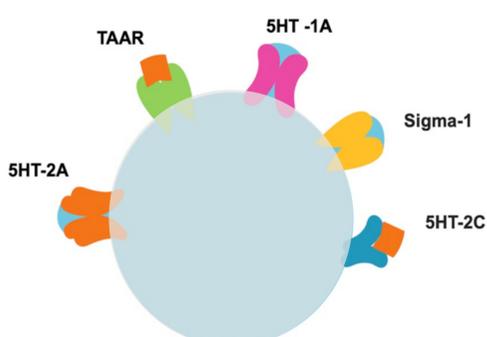
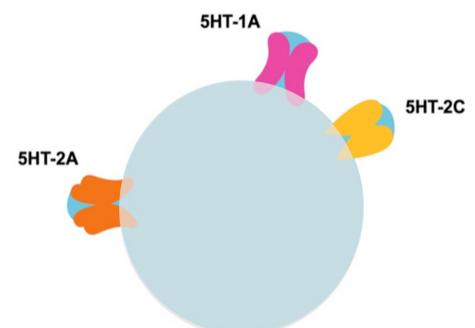


## Mechanism of Action for LSD, Psilocybin, and DMT [12]



LSD is a semi-synthetic tryptamine. LSD acts primarily upon 5-HT<sub>2A</sub> and 5-HT<sub>1A</sub> receptors, and partly upon the dopamine (DA) receptors D1 and D2 and the adrenergic  $\alpha_2$  receptors. This causes an increase in cortisol, oxytocin, and adrenaline levels.

Psilocybin is dephosphorylated by hepatic first-pass metabolism. Psilocybin acts primarily upon 5-HT<sub>2A</sub>, 5-HT<sub>1A</sub>, and 5-HT<sub>2C</sub> receptors.

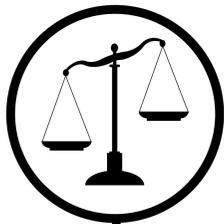


DMT acts primarily upon 5-HT<sub>2A</sub>, 5-HT<sub>2C</sub>, 5-HT<sub>1A</sub> receptors, sigma-1, and trace amine-associated receptors (TAARs). The sigma-1 agonist is responsible for immunomodulatory and anti-inflammatory properties, whereas TAARs are mediators of consciousness and perception.



# Legislation/Regulation

- Controlled substances have a higher-than-average potential for abuse or addiction. Therefore, their improper use can result in harm to public health or safety. That is why these drugs and their substances are regulated. Controlled substances and drugs are categorized into schedules.
- Psychedelics are one of the many drug classes classified as controlled substances.
- These controlled substances require specialized licensing, or a granted exemption from the governing authority to be handled legally.



## Canada

All legislative documents related to controlled substances are contained in the [Controlled Drugs and Substances Act](#), the [Narcotic Control Regulations](#), [Parts G and J of the Food and Drug Regulations](#), and the [Benzodiazepines and Other Targeted Substances Regulations](#).

The Controlled Drugs and Substance Act sets out [ten schedules](#) (2 repealed) for controlled substances including LSD, peyote, psilocybin, DMT, and MDMA.

Part G and J of the Food and Drug Regulations require authorization from Health Canada for controlled substances, such as psychedelics, to be regulated for possession, production, sale, transportation, and import and export for clinical trials or research purposes.

### [J.01.001](#) Restricted drug means

- (a) any substance that is set out in the schedule to Part J or anything that contains the substance
- (b) cocaine (benzoylecgonine) or any of its salts

[J.01.004](#) (1) The following persons are authorized to have a restricted drug in their possession:

- (a) a licensed dealer
- (b) a qualified investigator who possesses the drug for the purpose of conducting clinical testing or laboratory research in an institution
- (c) an inspector, member of the Royal Canadian Mounted Police, police constable, peace officer, member of the technical or scientific staff of the Government of Canada, the government of a province or a university in Canada who possesses the drug in connection with their employment
- (d) a person exempted under section 56 of the Act with respect to the possession of that drug
- (e) the Minister

Most psychedelics are categorized as Schedule 3 controlled substances. Schedule 3 includes LSD and psilocybin. MDMA and ketamine are listed under Schedule 1.

Failure to comply with laws may lead to punishments such as:

- Issuance of warning letters
- Requirement of corrective action plans
- Suspending and revoking licences, permits, or exemptions
- Imprisonment
- Fines





# Legislation/Regulation



USA

Legislative documents related to controlled substances are contained in the FDA sections [811 to 814](#) and in the FDA regulations [Title 21, Chapter II, Part 1308](#).

[812. \(a\)](#) contains the five schedules of controlled substances. The schedules established in this section are updated annually.

#### Schedule I

- High potential for abuse
- No currently accepted medical use in treatment in the United States
- Lack of accepted safety

#### Schedule II

- High potential for abuse
- There is accepted medical use in treatment in the United States
- Abuse may lead to severe psychological or physical dependence

#### Schedule III

- Potential for abuse less than schedules I and II drugs
- There is currently accepted medical use in treatment in the United States
- Abuse may lead to moderate or low physical dependence or high psychological dependence

#### Schedule IV

- Low potential for abuse
- There is currently accepted medical use in treatment in the United States
- Abuse may lead to limited physical dependence or psychological dependence

#### Schedule V

- Low potential for abuse
- There is currently accepted medical use in treatment in the United States
- Abuse may lead to limited physical dependence or psychological dependence

[812. \(c\)](#) sets out the list of controlled substances under Schedules I, II, III, IV, and V including LSD, peyote, psilocybin, DMT, and MDMA.

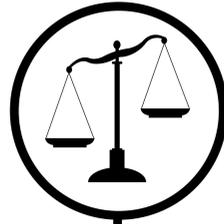
[821 to 832](#). Describes registration of manufacturers, distributors, and dispensers of controlled substances.

- Every person who manufactures, distributes, or dispenses a controlled substance, requires a registration issued by the Attorney General unless exempted by section 956 or under 1301.22 through 1301.26 of regulations.
- Each controlled substance has been assigned an “Administration Controlled Substances Code Number”
- Registration requirements are highlighted in section 823
- Labelling and packaging requirements are highlighted in section 825





# Legislation/Regulation



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## Europe

All legislative documents related to psychotropic substances are contained in the United Nations Convention on Psychotropic Substances.

The United Nations Convention on Psychotropic Substances sets out [four schedules](#) for controlled substances including

Schedule 1 – High risk of abuse, serious threat to public health which are of very little or no therapeutic value, including LSD, peyote, psilocybin, DMT, and MDMA

Schedule 2 – Risk of abuse, serious threat to public health with low or moderate therapeutic value

Schedule 3 – Risk of abuse, serious threat to public health with moderate or high therapeutic value

Schedule 4 – Risk of abuse, minor threat to public health with high therapeutic value

[Article 8](#). The manufacture of, trade (including export and import trade) in, and distribution of substances listed in Schedules II, III, and IV must be under licence or other similar control measures.

[Article 10](#). Warnings on packages, and advertising

- Each Party shall require directions for use, including cautions and warnings, to be indicated on the labels where practicable
- Each Party shall prohibit the advertisement of such substances to the general public

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## India

India has signed an agreement with the UN Single Convention on Narcotics Drugs 1961, The Convention on Psychotropic Substances, 1971, and The Convention on Illicit Traffic in Narcotic Drugs and Psychotropic Substances, 1988.

In addition, India is required to submit an annual report in accordance with Form "P" to the International Narcotics Control Board (INCB). This report must contain information on quantities manufactured, quantities exported to and imported from each country or region, and stocks held by manufacturers in relation to psychotropic substances.

The [Central Bureau of Narcotics](#) describes the use of psychotropic substances for medical and scientific purposes as “indispensable.” The list of psychotropic substances is specified in the schedule under the [Narcotic Drugs and Psychotropic Substances \(NDPS\) Act, 1985](#). The regulations around the [manufacturing of psychotropic substances](#) depends on its schedule.

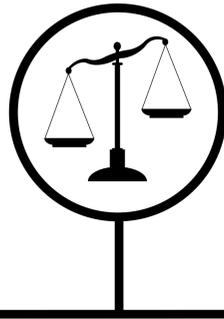
Schedule I – manufacture is completely prohibited

Schedule III – manufacture for export only is permitted

Any psychotropic substance not listed in Schedule I and Schedule III – manufactured for sale in India or for export is permitted with a license from the State Drugs Controller under the Drugs and Cosmetics Act and Rules



# Legislation/Regulation



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## Australia

All legislative documents related to controlled substances are contained in the [Therapeutic Goods Administration \(TGA\)](#) including the [Poisons Standard](#), the import and export regulations, the [Narcotic Drugs Act 1967](#), the [Criminal Code Act 1995](#).

- The Poisons Standard is a legislative instrument that sets out schedules to classify medicines and poisons. The regulatory requirements that the Poisons Standard control include certain advertising, labelling, packaging containers, storage, disposal, record-keeping, sale, supply and possession of poisons and is determined by the schedule classification of the medicine or poison.
- The Narcotic Drugs Act 1967 puts into practise certain of Australia's obligations under the [Single Convention on Narcotic Drugs, 1961](#). The Act enables a licensing and permit scheme that regulates the manufacture of drugs covered by the Convention. The act also permits authorities to enforce compliance.

A list of controlled substances <https://www.odc.gov.au/ws-lps-index>.

The laws regarding controlled drugs in Australia vary on the territory, while others are federal. Refer to Australia's Government [page](#) for more information.



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## Japan

Japan has signed an agreement with the UN Single Convention on Narcotics Drugs 1961, The Convention on Psychotropic Substances, 1971, and The Convention on Illicit Traffic in Narcotic Drugs and Psychotropic Substances, 1988. In addition, Japan has enacted the [Narcotics and Psychotropics Control Act](#) and the Law Concerning Special Provisions for the Narcotics and Psychotropics Control Act, for the further prevention of activities encouraging illicit conduct or involving controlled substances such as psychedelics.

Lysergic acid is classified as a narcotic or psychotropic raw material under the Appended Table IV

- A person seeking to become an importer, exporter, manufacturer, or retailer of a narcotic or psychotropic raw material must file a business notification

Refer to Japan's [Pharmaceutical Administration and Regulations](#) and government [page](#) for more information.



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## China

There are limited resources available in English in regard to the measures for the control of psychotropic drugs in China. Refer to China's [Medicine Administration of the People's Republic of China regulations](#) for some information.

- Article 3. Psychotropic drugs are classified into category I and II in accordance with the extent of drug dependence and hazard.
- Article 4. Psychotropic drugs shall only be produced if appointed by the Ministry of Public Health and the State Administration for Medicine.
- Article 15 -17. The prescription of psychotropic drugs is allowed by doctors based on true need in treatment.



# Dalton's Services

Dalton has easy access to over 3,000 high-quality research molecules including controlled drugs. As an FDA, HC, and EMA approved company and a controlled drug license holder, Dalton proudly contributes to the development of psychotherapy-based medicines for mental health. Dalton is dedicated to fighting mental health through the medical use of controlled substances in psychotherapy. For dosage formulation development and commercialization of your psychedelic drug product or other controlled substances visit our [controlled substance services](#).

For a full list of our services, please visit <https://www.dalton.com>.



## From Sacred Plant to Psychotherapy

1943

Scientific discovery of psychedelics

Discovery of psychoactive properties of LSD by Hoffman

[8]

1970

Controlled Substance Act

The US passed the Controlled Substance Act in 1970 in order to regulate the manufacture, importation, possession, use, and distribution of certain drugs, such as narcotics and hallucinogens. This act was established to minimize substance abuse. [8]

Historically

Sociocultural and ritual use of psychedelics

For thousands of years, psychedelic plants have shaped indigenous people's spiritual-cultural practices and many other religious ceremonies. [13] For example, 'Soma' the active component of a hallucinogenic mushroom, appears throughout Sanskrit texts in the Hindu religion. [13]

1960

Recreational use and abuse of psychedelics

Youth who were part of the counterculture movement in the late 1960s, known as hippies, were well known for their recreational use of psychedelic drugs. [14]

Now

Potential psychotherapeutics implications of psychedelics [15]

When the medical use of cannabis became legalized in certain countries, governments became more open-minded towards the medical benefits of stigmatized illegal and recreational drugs. Now, scientists are studying the potential medical benefits of psychedelics, such as psilocybin.

Clinical studies have shown that psychedelics may play a major role in the future of mental health. While this is an exciting opportunity, the intellectual property rights of indigenous people for their historical use of psychedelics must be considered and protected.



# Psychedelic Companies

## Public Psychedelics Companies

Compass Pathways

MindMed

Cybin Corp

Field Trip Health, Inc.

Revive Therapeutics Ltd.

Numinus

HAVN Life Sciences

Mydecine Innovations Group

Red Light Holland

Champignon Brands Inc.

Mindset Pharma

M2BIO

Neonmind Biosciences

Roadman Investments Corp.

Bright Minds Biosciences

Silo Wellness

Novamind

Psychedelics ETFs

Ehave Inc

Champignon Brands Inc.

Mind Cure Health Inc.

Entheon Biomedical

Better Plant Sciences

Tryp Therapeutics

New Wave Holdings

Aion Therapeutic

Lobe Sciences

PharmaTher

Hollister Biosciences

## Private Psychedelics Companies

ATAI Life Sciences

Awakn Life Sciences

Beckley Psytech

Bexson Biomedical

CaaMTech

CB Therapeutics

Delix Therapeutics

Diamond Therapeutics

Earth Resonance

Eleusis

Gilgamesh Pharmaceutical

MagicMed Industries

Octarine Bio

Psilera Bioscience

PsyBio Therapeutics

Psygen

Small Pharma

Tactogen

Universal Ibogaine

Wake Network





# Psychedelic News and Ecology

## Psychedelic Latest News



01

In August 2020, four terminally ill cancer patients in Canada received special access approval for the use of psilocybin as a psychedelic therapy to treat their anxiety. For the full story click [here](#).

02

In December 2020, Health Canada granted permission for 16 healthcare professionals to have access to psilocybin for personal training. For the full story click [here](#).

03

In May 2019, Colorado became the first state in the U.S. to decriminalize the psychedelic drug psilocybin. For the full story click [here](#).

04

In November 2020, Oregon became the first state in the U.S. to decriminalize the possession of hard drugs including the psychedelic drug LSD. For the full story click [here](#).

05

In February 2021, California introduced a bill that would decriminalize psychedelics like LSD, psilocybin, and MDMA for personal and therapeutic use. The bill excludes the use of peyote. For the full story click [here](#).

## Psychedelics and Ecology

There is a high global demand for psychedelics due to their increasing recreational use. Unfortunately, natural sources of psychedelics are often derived from endangered animal and plant species or involve animal cruelty. Mescaline, a naturally occurring psychedelic derived from the Peyote cactus (*Lophophora williamsii*) is federally listed as an endangered and threatened species, with a cultivation period of up to 13 years. (16) An eco-friendly alternative to peyote is the naturally occurring mescaline found in the stable San Pedro cactus (*Echinopsis pachanoi*) plant population. The psychedelic 5-MeO-DMT is also derived from an endangered and threatened species. (17) 5-MeO-DMT is extracted from the venom glands of the endangered and threatened Colorado River toad, also known as the Sonoran Desert toad (*Incilius alvarius*). (18) An eco-friendly alternative to 5-MeO-DMT derived from the Colorado River toad is synthetic 5-MeO-DMT. Although most synthetic drugs are safer and more effective than all-natural compounds, due to their consistency in potency and precise dosage form, some synthetic drugs may not be environmentally friendly. For instance, the sources required for the synthesis of MDMA involve deforestation. (19) To mitigate the ethical and ecological concerns around psychedelics, research and treatment of psychedelics should center on psychedelics derived from species that are readily available and easily cultivated, such as psilocybin.

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