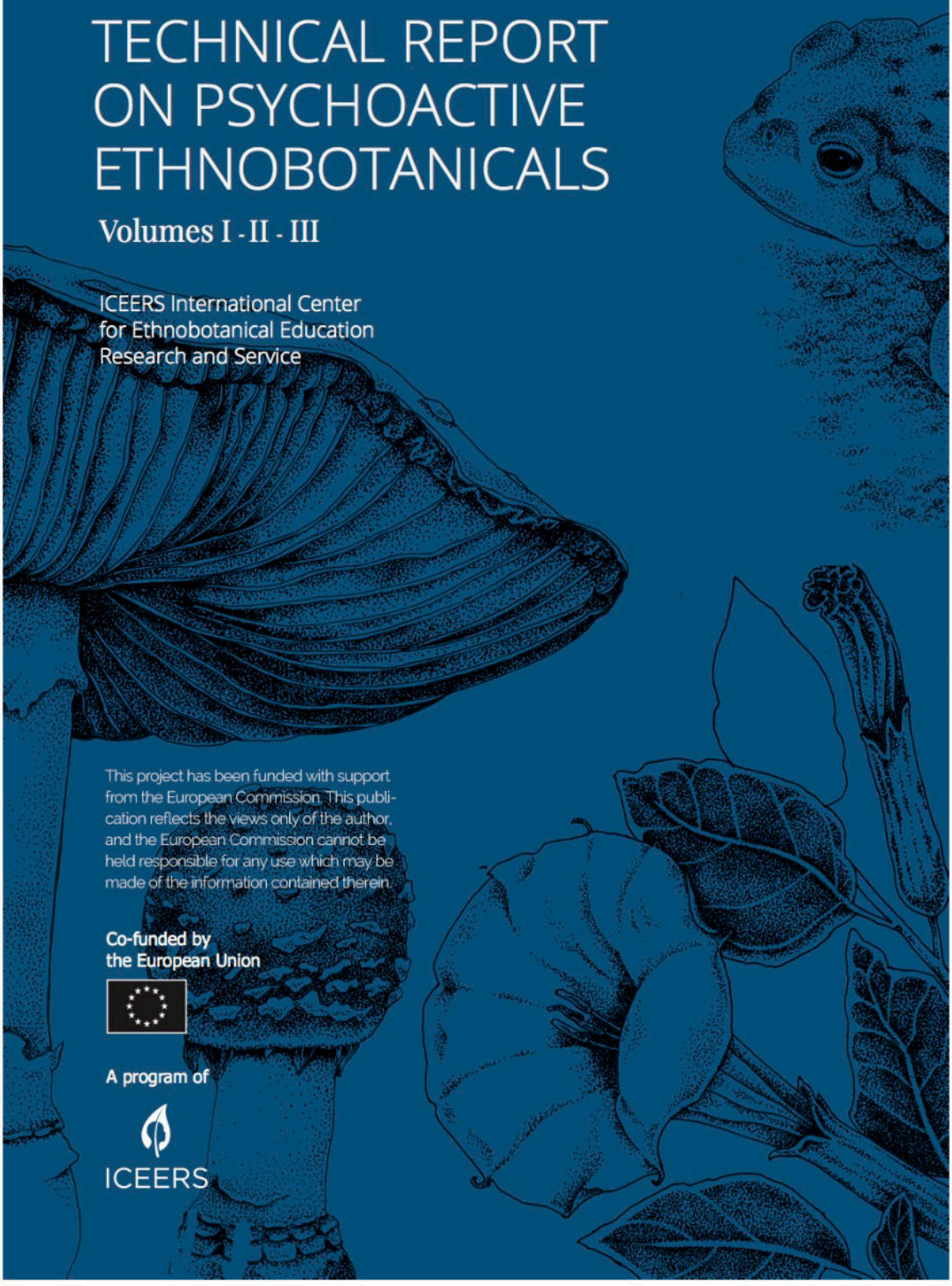
TECHNICAL REPORT ON PSYCHOACTIVE ETHNOBOTANICALS

Volumes I - II - III

ICEERS International Center
for Ethnobotanical Education
Research and Service



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SALVIA DIVINORUM

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The effects of the Hierba Pastora have been used by Mazatec Indians since ancient times to treat diseases and for divinatory purposes. The psychoactive compound *Salvia divinorum* contains, Salvinorin A, is the most potent naturally occurring psychoactive substance known.

BASIC INFO

Salvia divinorum is a perennial plant native to the Mazatec areas of the Sierra Madre Oriental Mountains of Mexico. Its habitat is tropical forests, where it grows between 300 and 800 meters above sea level. It belongs to the Lamiaceae family, and is mainly reproduced by cuttings since it rarely produces seeds.

It is known by different names: Ska Pastora, Pastora leaves, Maria Pastora leaves, or simply Salvia. It has been used by the Mazatec Indians for purposes of divination, as well as to treat various diseases such as anemia, rheumatism, headache, stomach swelling and diarrhea.

S. divinorum contains a potent psychoactive substance called Salvinorin A that produces psychedelic and dissociative effects in very low doses, varying in duration depending on the route of administration, usually lasting between fifteen minutes and two hours. Salvinorin A is the most potent natural psychoactive substance known.

S. divinorum is used either orally, chewed, or smoked in the form of extracts.

ORIGIN/HISTORY

The use of Ska Pastora is associated with the use of psilocybin mushrooms in Mazatec cults. It is unknown whether *S. divinorum* was used in the pre-Hispanic era, although some authors have hypothesized that the Aztecs may have used it and called it “Pipiltzintzintli”, but this speculation has its detractors and other plants like Cannabis and Rivea corymbosa (Ololihuiqui) could also be candidates for the Aztecan “Pipiltzintzintli”. In addition to shamanic, divinatory and magico-religious uses, *S. divinorum* has also been used for its medicinal properties.

Ska Pastora has been used in divination and healing rituals, similar to psilocybin mushrooms. Maria Sabina told Wasson and Hofmann (the discoverers of its Mazatec usage) that *Salvia divinorum* was used in times when there was a shortage of mushrooms. Some sources that have done later fieldwork point out that the use of *S. divinorum* may be more widespread than originally believed, even in times when mushrooms were abundant.

Rituals traditionally take place at night, in silent darkness. The leaves of the plant are chewed making a kind of cylinder with them. Participants chew the leaves in pairs, and the juice produced is not swallowed but kept in the mouth to be absorbed by the mucous membranes. Leander Valdés published his experiences on the current use of *Salvia divinorum* among the Mazatec Indians and included descriptions of the rituals as well as the effects of *Salvia*.

Once the effects begin, people lie down and remain quiet and silent. Visions often appear in this state. The Salvia ritual usually lasts less than two hours.

CHEMICAL COMPOSITION AND DOSAGE

The leaves of *S. divinorum* contain two diterpenes called Salvinorin A and Salvinorin B (also known as divinorin A and divinorin B). They also contain other substances that are not clearly identified.

Salvinorin A is the most potent natural psychedelic substance known. It is about 10 times more potent than psilocybin. Its chemical formula is $C_{23}H_{28}O_8$ and it does not contain nitrogen, so it is not an alkaloid. At the pharmacological level it acts as a selective agonist for kappa opioid receptors, which differentiates it from other

psychedelic compounds that act mainly on the serotonergic system, specifically binding to the 5HT2A receptors. Salvinorin A is therefore quite an unusual compound.

Doses of Salvinorin A that produce psychoactive effects start at 150 micrograms (or millionths of a gram). Common doses are between 150 and 500 micrograms.

Dried *S. divinorum* can be found on the market, although its availability in the form of extracts is more common. These extracts are more potent than dried leaves, so a much smaller amount is required to achieve psychoactive effects. Fresh leaves are usually only found in places where *S. divinorum* is grown and are not usually available in other markets.

The traditional route of administration is usually the chewing of fresh or dried leaves, as well as the ingestion of leaf infusions. In current contexts in the western world, the most common route of administration is the smoking of extracts.

An approximate summary of the usual doses is as follows:

Smoked or vaporized route. Dosage of leaves

» Low dose: 0.25 grams
» Average dose: 0.5 grams
» High dose: 0.75 grams

Smoked or vaporized route. Dosage of 5x extract

» Low dose: 0.05 - 0.1 g
» Average dose: 0.08 - 0.15 g
» High dose: 0.01 - 0.025

Smoked or vaporized route. Dosage of Pure Salvinorin A

» Low dose: 75 - 100 µg (dose in micrograms, 1000 micrograms, µg = 1 milligram, mg)
» Average dose: 200 - 400 µg
» High dose: > 500 µg

Sublingual/chewed route. Dosage of leaves

» Low dose: 10 g of fresh leaves / 2 g of dried leaves
» Average dose: 30 g of fresh leaves / 6 g of dry leaves
» High dose: 50 g of fresh leaves / 10 g of dried leaves

Oral route: infusion of crushed leaves (in pairs of leaves, traditional use)

» Low dose: less than 20 pairs (40 leaves)
» Average dose: from 20 to 60 pairs
» High dose: 60 to 80 pairs

EFFECTS

The effects of *S. divinorum* vary greatly depending on the dose and, above all, on the way it is administered.

Some common effects are intense changes in perception and mood, as well as somatic sensations (pressure in certain areas of the body, applied force on the body, floating, body warmth) the sensation of merging with objects in the environment, changes in perceptions of spatial and temporal dimensions, as well as deep dissociative states, geometric visions or landscapes of a dream-like nature and extra-corporeal experiences.

The positive effects that some users report include: increased aesthetic appreciation of the environment, feeling calm, synesthesia, visions, feelings of insight and spiritual experiences, among others.

Negative or unwanted effects include: loss of control over the experience, difficulty in integrating experiences, panic attacks, fear, terror, agitation or loss of motor control, dizziness, paranoia, temporary loss of the ability to communicate and amnesia. These types of negative effects are more easily produced with potent extracts, occurring less frequently when the leaf is chewed.

The effects when the leaves are chewed or infused usually appear within ten minutes, and are maintained for a further forty-five minutes. There are reports of people claiming to have experienced effects hours after chewing and that the total duration was over four hours. However, the doses used in these cases usually vary from the five pairs of leaves (a non-psychotropic dose, traditionally used to treat anemia, regulate excretory functions and stomach swelling) up to fifty pairs.

The chewed or infused leaves produce a smoother effect,

including visions with closed eyes. It is considered necessary to be in silent darkness in order to appreciate the intensity of the experience, as it may be difficult to perceive the effects otherwise.

When the plant is consumed by smoking or inhaling the vapors the effects are established much faster and the intensity is much greater. The experience begins within seconds of inhalation, its peak is sustained for 2-20 minutes and usually lasts for about 30 minutes, with residual effects up to one hour. High doses can produce strange effects, such as the sensation of a "doubling" of space-time, radical changes in perspective from which reality is experienced, loss of consciousness of the individual self or "I", forgetting that a substance has been consumed, sensations of energies in movement, pressure, the sensation of entering other dimensions, profound alterations to the perception of time... Experiences can be pleasant, but also frightening given their intensity and strangeness. The frequency of difficult, confusing or frightening experiences seems to be relatively high among users, and many people decide not to reuse Salvia after a single experience. Some users also report that the use of Salvia occasionally causes a strong feeling of anxiety and paranoia.

Occasionally people will move about spontaneously during the experience, and even get up and walk without being aware of it. This implies the risk of falls and accidents.

LEGAL STATUS

Neither *S. divinorum* nor salvinorin A are included on the lists of United Nations conventions on drugs.

However, some countries have included *S. divinorum* and salvinorin A in their lists of controlled substances. These countries are: Australia, Japan and some states of the United States; and in Europe: Italy, Lithuania, Latvia, Sweden, Romania, Belgium and Denmark.

In countries such as Norway, Finland and Estonia, the plant is controlled under drug legislation. Other countries have only regulated the plant: Spain, Poland, Germany and Croatia.

PREVALENCE OF USE

There is little conclusive information about the prevalence of *S. divinorum* use in different European countries. There are some studies that have documented data on Salvia use in different countries and contexts. In general Salvia is a little used substance, and among those who have used it the frequency of its use is also very limited.

Studies of the United States population indicate that Salvia is mainly used by people in the 18-25 age group, principally males who are active consumers of other psychoactive substances, predominantly stimulants and psychedelics. According to these studies 1.3% of the respondents had used Salvia in their lifetime in 2008.

According to the EMCDDA, about 3.2% of those who regularly go to electronic music dance clubs have used *S. divinorum* on some occasion in the last month, and 29.2% have used it in their lifetime. These results cannot be extrapolated either to the general population or to other dance club users, due to the bias of online surveys.

According to EMCDDA data from 2014, 0.4% of adolescents in Spain between the ages of 14 and 18 have tried Salvia in the last 12 months and 0.6% has done so in their lifetime.

The Global Drug Survey collects data for 2017, and 6.1% of those surveyed claim to have used Salvia at some point in their lifetime. This is an online questionnaire, which people access and answer voluntarily, so there may be a bias in the type of people who have filled out the form. Salvia appears in thirteenth position of the most consumed drugs, ahead of crack, methylphenidate, methamphetamine, opium, DMT and other substances.

In any case the use of *S. divinorum* seems to be clearly experimental, and it is not used socially, recreationally or as a substance for partying. Also, the use of *S. divinorum* seems to have a low continuation rate, and about half of people who consume it once have no intention of repeating the experience.

HEALTH AND RISK REDUCTION

The potency of the leaves is difficult to gauge, and extracts can vary widely depending on the supplier. Therefore dosing can be complicated, and there is a risk of overdose, in particular using smoked extracts.

It is important to calculate the dose well using a precision scale, and be cautious with the amounts used. The use of *S. divinorum* produces a tolerance, so people who use it frequently or on successive occasions need to increase the dose to experience effects.

An experience with *S. divinorum* can be frightening in some cases and involve situations of fear, panic and extreme states of confusion. At high doses it is common to be unaware of the environment, or to forget having smoked Salvia. There is a clear danger of getting up during the experience and having an accident. It is highly recommended to have a sober caretaker present the entire time during experiences with *S. divinorum*.

The context or setting is also important as some users report difficult experiences due to the environment itself. Safe, calm environments, with little stimuli, away from crowds, free of dangerous objects or obstacles and with a sober caretaker will reduce the risks of accidents and negative experiences.

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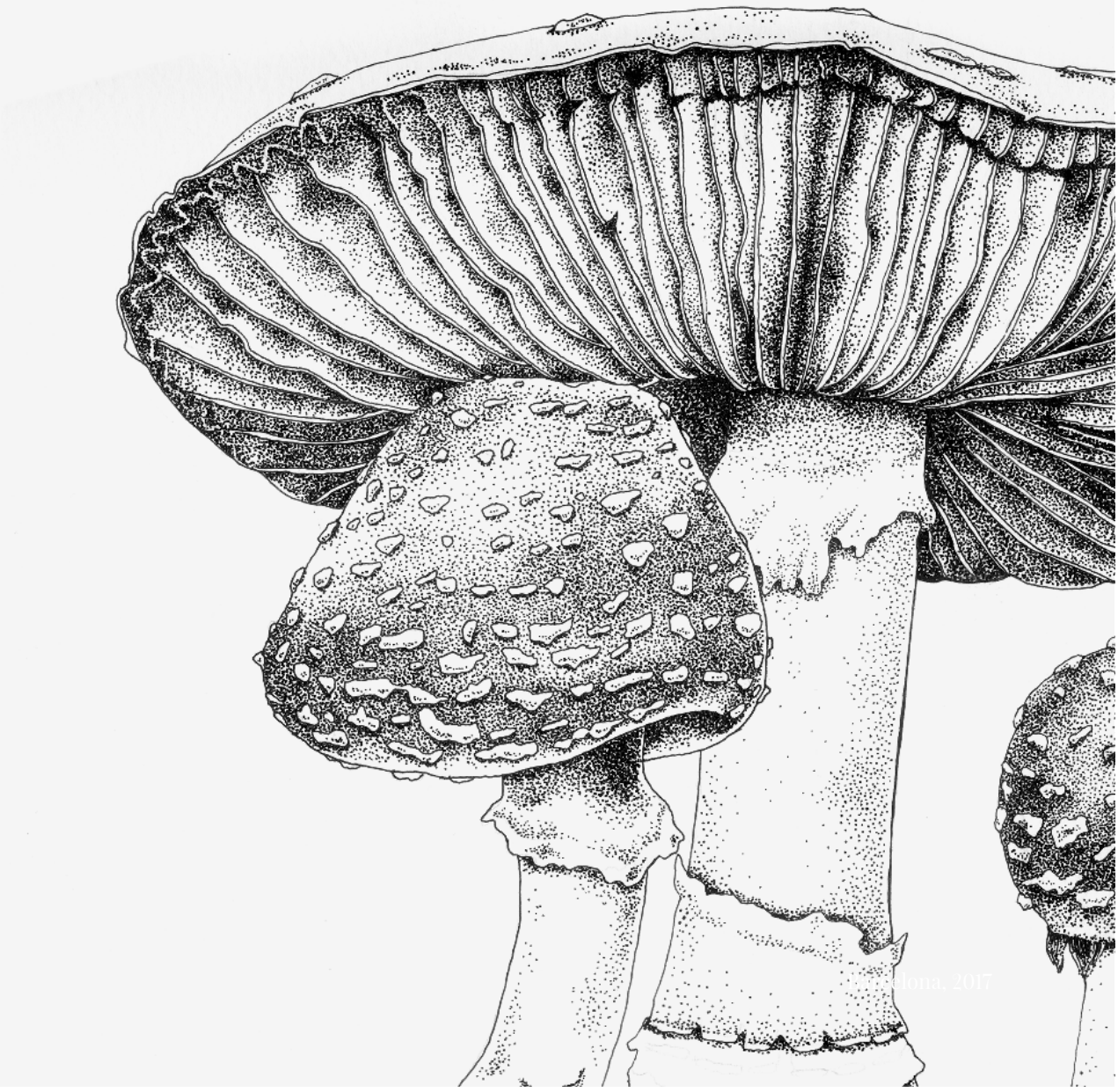

AMANITA MUSCARIA

Peoples of America, Europe and Asia have traditionally used *Amanita muscaria* for centuries with divinatory, shamanic and religious purposes due to its psychoactive effects.

BASIC INFO

Amanita muscaria (and another similar variety, *Amanita pantherina*) is a mushroom of the agaricales order that appears in very broad habitats of the temperate and boreal zones of the Northern Hemisphere. It grows both in low altitudes and high mountainous areas, especially in coniferous forests such as beech, birch, fir and black pine. It usually appears during the end of summer months and is especially prevalent in autumn.

Its appearance is well known by the red color of the cap, covered with white dots, as well as the white stem.

This mushroom contains two psychoactive alkaloids, ibotenic acid and muscimol, in addition to many other alkaloids. It has been used since antiquity as an intoxicating substance as well as in shamanic contexts and divination.

The name *Amanita muscaria* comes from the paralyzing effect it has on some insects. It is known by other names such as flyswatter mushroom, falsa oronja, reig bord or farinera borda in Catalan, and fly agaric in English.

ORIGIN/HISTORY

Historical records such as cave paintings, wood carvings and sculptures suggest that the psychoactive effects of *A. muscaria* have been known since ancient times on all continents, and similar practices have been observed regarding the use of *A. muscaria* in groups both geographically and culturally distant. *A. muscaria* has been used for religious, divination, therapeutic and social purposes.

The first evidence of the use of *A. muscaria* as an intoxicant is based on linguistic analyses of North Asian languages from 4000 BC, in which the roots of the words "drunkenness" and the name attributed to this mushroom appear to be the same. Polychromatic paintings have been found on Saharan rocks dating back to the Paleolithic period; depictions of what appear to be *A. muscaria* mushrooms.

The fungus grows naturally in the highlands of Mesoamerica and some mushroom myths and sculptures suggest the use of *A. muscaria* in Guatemala and southern Mexico at the time of creation of the Mayan civilization, around 1500 - 1000 BC. Some symbolic similarities have been found in Guatemalan and Asian populations relating to the belief that the mushroom is born in places where lightning strikes. These parallels could be explained by the migrations that likely occurred from the Asian continent to the Americas via the Bering Strait, thus the knowledge about the use of *A. muscaria* would have been relayed.

There is further evidence of its use in North America by the Dogrib Athabasca tribes in the Mackenzie Mountains in Canada as well as in the ceremonial practices of the Ojibwa and Ahnishinuabeg Indians in the Lake Michigan area of the United States, who referred to *A. muscaria* by the name of miskwedo and whose practices have survived until at least the end of the 20th century.

The first Western report on the use of *A. muscaria* was made by Filip Johan von Strahlenberg, a Swedish soldier who, in 1730, was imprisoned for twelve years in Siberia. He observed how *A. muscaria* was used as an intoxicant in shamanic contexts. Currently the Ostyak and Vogul tribes, west of Siberia, and the Kamchadal, Koryak, and Chukchi tribes in the east, continue to use *A. muscaria* in their rites.

These Siberian tribes relied exclusively on *A. muscaria* as an intoxicating substance until the introduction of alcohol by the Russians. They collected the *A. muscaria*, dried it in the sun and consumed it either whole, in a water or

reindeer milk extraction, or mixed it with plant juices to sweeten its flavor.

These tribes also exhibited the practice of consuming the urine of people who had eaten *A. muscaria*, as they learned that the alkaloids of *A. muscaria* are eliminated unchanged through urine, so they remain active and can be reused for up to four or five cycles.

As for *Amanita pantherina,* some native North American groups use it for magico-religious purposes in the western part of the state of Washington.

CHEMICAL COMPOSITION AND DOSAGE

A. muscaria contains a high quantity of alkaloids and its pharmacology is complex and not fully understood. The most relevant alkaloids are ibotenic acid, muscimol, muscarine and muscazone.

For some time, muscarine was believed to be the psychoactive alkaloid of the *A. muscaria*, but in 1964 independent researchers in Japan, England, and Switzerland isolated ibotenic acid and muscimol, and discovered their psychoactive properties. Muscarine is the alkaloid responsible for undesired effects and the feeling of intoxication (discomfort, upset stomach and vomiting).

The quantity and proportion of alkaloids contained in the mushroom depends on several factors. Mushrooms collected at higher altitudes appear to have higher concentrations of ibotenic acid/muscimol, and those collected at lower altitudes, more muscarine.

Ibotenic acid is a rather unstable molecule, which is converted into muscimol by exposure to temperature and other factors. Thus, the dry mushroom is usually more powerful than the fresh specimen, because during the drying process the ibotenic acid is decarboxylated into muscimol. Ibotenic acid has stimulant effects, while muscimol has more depressant effects.

Dosage of Ibotenic Acid: This alkaloid causes psychoactive effects in doses of 50 - 100mg.

Dosage of Muscimol: Equivalent doses are in the ranges of 10 - 15mg. Thus muscimol is more potent than ibotenic acid.

Dosage of *A. muscaria*: The concentrations of alkaloids are highly variable depending on the height and specific ecosystem where the mushroom grows, so the dosage is very difficult to determine and the doses indicated here are merely orientative.

» Low dose: a small or medium size cap.
» Average dose: from 1 to 3 medium size caps.
» High dose: 2 or more medium size caps.

EFFECTS

Both muscimol and ibotenic acid have psychotropic effects. After oral administration, the effects take quite a long time to appear, and it usually takes 2 to 3 hours to reach the maximum effects. The duration of the effects is about 6 or 8 hours, depending on the dose.

The nature of the effects can be highly variable, also depending on the dose, as well as the variety and personal differences.

Effects may include:

» A first phase in which there is stimulation, increased energy and muscular vigor (not always)
» A second phase in which there is decay, tranquility and drowsiness.
» A third phase in which the psychedelic effects appear and there may be experiences of a mystical nature, awareness of non-ordinary realities, blissful or terrifying sensations.
» Visual Distortions
» Loss of balance
» Muscle spasms
» Experiences of a dream-like nature
» Dizziness
» Visual and auditory impairment
» Difficulty concentrating on external tasks

AMANITA MUSCARIA

» Sensation of macropsia and/or micropsia (perceiving objects as either very large or very small)
» Nausea and vomiting

Both *A. muscaria* and *A. phanterina* contain ibotenic acid and muscimol, although each species contains these active ingredients in different concentrations, so the intoxication is also different. *A. muscaria* contains more excitatory ibotenic acid and less of the depressant muscimol compared to *A. pantherina*. For this reason, poisonings with *A. muscaria* present with more confusion and agitation compared to *A. pantherina* poisonings, which most commonly present with comatose symptoms.

LEGAL STATUS

A. muscaria and the other varieties of *Amanita* are not controlled in most countries.

In the Netherlands and the United Kingdom, however, possession, purchase and sale are prohibited. In Romania, *A. muscaria* has also been prohibited since 2010, although previously it could be gathered and sold and was available in *smart shops.*

HEALTH AND RISK REDUCTION

It is essential to make accurate identifications of fungi, since there are different varieties that vary widely in potency, and there are other species that can be confused with *A. muscaria,* and especially with *A. pantherina*, that are lethal, as is the case with *A. phalloides.*

A. muscaria: can reach up to 18cm high, has a red cap (or orange in older specimens) and usually has white spots. The blades under the cap are white.

A. pantherina: similar to *A. muscaria*, but the cap usually has a color ranging from cream to brown. It can also be confused with *A. rubescens* (edible).

A. phalloides (FATAL): This highly poisonous mushroom has a whitish or greenish cap. It does not usually have white spots on its cap.

WAYS OF USE

A. muscaria has traditionally been washed and dried after collection, and the stem is usually discarded since it can contain a large amount of larvae. Drying is recommended to reduce intestinal discomfort. The dried mushroom can be eaten directly, cut up, or by making an infusion with hot water, filtering it and drinking the water. It seems that the second method reduces stomach discomfort.

The effects of *A. muscaria* can take up to 2 or 3 hours to appear. Being very careful with the amount ingested is recommended (no more than a small or medium cap), as is waiting a few hours to see the progression of the effects. The potency of the mushroom can be highly variable, so be careful with the dosage.

There is an anecdotal report of Mexican shamans using the cuticle (red skin of the cap), which is separated from the rest of the cap while the mushroom is fresh, allowed to dry and then smoked. The effects appear more quickly and their duration is shorter by this route, although there are no comprehensive descriptions of dosage or effects. It appears that the intensity is lower than when the mushroom is ingested orally.

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DATURA STRAMONIUM

DATURA STRAMONIUM

Solanaceous plants in the Datura family contain psychoactive alkaloids that can cause hallucinations and dangerous toxic effects. These plants have been used since antiquity for medicinal purposes and in magico-religious rituals.

BASIC INFO

Datura stramonium is a wild plant of the Solanaceae family. It is found in both hemispheres, in areas of temperate, subtropical and tropical climates. It is a plant native to Asia, but it also grows in North America and Europe.

D. stramonium, like many Solanaceae, contains tropane alkaloids that are toxic and dangerous, such as atropine, hyoscyamine and scopolamine. Plants that are similar to *D. stramonium* are *Datura metel* and *Datura inoxia*.

Solanaceae have been used traditionally in different cultures for medical and healing purposes, as well as for rituals of initiation, divination and magico-religious rites. These plants include the different species of daturas such as henbane (*Hyoscyamus niger*), mandrake, and the different varieties of brugmansias (the species of Datura native to South America).

ORIGIN/HISTORY

D. stramonium is a plant native to the deserts of southeastern North America and Central and South America, Europe, Asia and Africa. It is found mainly in the areas near the Himalayas, from Kashmir to Sikkim, at altitudes of up to 2700 meters. It reproduces by means of seeds and grows in woody logs reaching a height of up to 2 meters.

Different cultures have used the varieties of Datura for their medicinal and intoxicating properties.

In Tibet the entire plant is used. The seeds have been used to treat joint pain, asthma and excessive coughing, gastric convulsions and strokes. The flowers have been used as an anesthetic.

In India the use of different varieties of datura, particularly *D. metel* has been established. It has been used as a visionary and intoxicating plant, associated with the cult of the god Shiva, and its risks were well-known. In other parts of Asia the plant has been used as an addition to alcoholic beverages to increase their intoxicating properties. In other places the seeds of the Datura have been mixed with Cannabis for their inhaled use. *D. stramonium* is part of the Ayurvedic pharmacopoeia.

The intoxicating and medicinal properties of Datura are also known in Africa. It has been used as an addition to Pombe, a local alcoholic beverage from Tanzania, to increase its intoxicating capacity. Leaves are smoked to relieve asthma attacks and lung problems.

There are indications that *D. stramonium* was already being used in Europe in the Paleolithic era. Residues of fermented beverages containing hyoscyamine have been found in pots dated to 3000 BC, used in funeral contexts. In medieval Europe it is known that plants related to Daturas were used, such as mandrake and henbane, which contain the same alkaloids. These plants were used for their medicinal properties, and also to induce visions. The visions and experiences induced by these plants as well as the methods of administration in ointments have been correlated to the experiences of medieval witches "flying" on brooms. These practices were condemned by the Catholic Inquisition, and the traditional use of these plants virtually disappeared.

In the New World, different varieties of Daturas, called toloache (*D. inoxia*), have been used in Mexico, both for magico-religious and medicinal uses, especially the application of ointments to reduce rheumatic pain and as an anti-inflammatory, as well as in initiation rites.

In Colombia, Ecuador and Peru, different ethnic groups have used brugmansia species, plants of the Datura genus that contain the same alkaloids for their divinatory qualities and for initiatory rites of the young.

DATURA STRAMONIUM

SUMMARY OF TRADITIONAL USES OF DATURA

D. stramonium has been used to treat unique problems: leaf juice is applied to the ear in cases of pain, leaves processed in oils or ointments have been used for muscle and rheumatic pains, swellings, injuries, wounds and bleeding. It is also used for the treatment of baldness and dandruff. Vapors and smoke from seeds and leaves have been used to relieve asthma and lung problems.

In Ayurveda, *D. stramonium* has been used to treat ulcers, wounds, inflammations, rheumatism, gout, sciatica, fever, asthma, bronchitis and toothaches.

D. stramonium has also been used as an anti-parasitic and insect repellent, both the plant as well as infusions made with its leaves.

CHEMICAL COMPOSITION AND DOSAGE

The chemical composition of the different varieties of Datura has been researched since 1930. The main tropane alkaloids containing *D. stramonium* are atropine, scopolamine and hyoscyamine. Daturas also contain small amounts of other alkaloids such as noratropine, apotropine, meteloidine, norscopolamine and aposcopolamine.

The dosage of Datura and other Solanaceae is extremely difficult to determine. Different parts of the plant contain different amounts of alkaloids and their concentration may vary depending on the time of year, variety and habitat. In general, the seeds are the part of the plant that contains the highest concentration of alkaloids.

The doses of atropine and scopolamine used in medicine are on the order of milligrams or tenths of a milligram, so accuracy in dosing is essential. With plants a precise dosage is impossible to determine and it is easy to overdose, including all the dangers that this can entail. Therefore the recommendation is not to use these plants at all.

EFFECTS

The toxic effects of Datura have been observed and studied since accidental poisoning with the plant is relatively frequent in places like India, and there have also been cases of poisoning and death in the United States and Europe.

The alkaloids related to poisoning appear to be scopolamine and its derivatives.

The effects of Datura intoxication include delusions, agitation and convulsions, mydriasis (dilated pupils), blurred vision, photophobia or hypersensitivity to light, dry mouth and other mucous membranes, extreme thirst, tachycardia, nausea and vomiting, difficulty swallowing and speaking, hypertension, increased body temperature, loss of consciousness and in some cases coma.

During an experience with Datura, hallucinations and real delusions usually occur, meaning there is no awareness that what is being experienced is due to the substance, and it is perceived as objective reality. Therefore, there is a risk of engaging in inappropriate behavior, erratic interaction with the environment, and causing or suffering accidents.

The onset of effects begins between 20 minutes and 4 hours after ingestion, depending on the route of administration, the dose ingested and the part of the plant used, as well as the method of preparation. Effects can last for several hours, and reports of people who have been intoxicated for 24-48 hours or even more are common.

After a Datura experience people usually have amnesia regarding what happened.

Many of the deaths attributed to Daturas were not caused by the direct effects of the plant, but by dehydration as people are in a delirious state for hours in extremely hot climates.

DATURA STRAMONIUM

LEGAL STATUS

Neither *Datura stramonium* nor other varieties of Daturas, brugmansias, henbane or plants containing tropane alkaloids such as atropine or scopolamine are controlled in most countries.

HEALTH AND RISK REDUCTION

Although the use of Datura and other Solanaceae has been conducted for medical, religious and ritual purposes in various cultures, and it is still in use today, the risks of poisoning by atropine, scopolamine and hyoscyamine are very high, and may involve accidents, irreversible physical and psychological problems and even death.

In the cultures that use these substances, their danger is recognized as is the absolute necessity that those who handle these plants have profound knowledge about them. Only highly experienced shamans utilize Datura.

Very small amounts of leaves, flowers or seeds can have dramatic effects that cause psychological problems (delusions, terrifying experiences, psychotic states of uncertain duration...) as well as physical ones (cardiovascular problems, cardiac arrest, convulsions, anaphylactic shock, falls, drownings...). Cases of death have been documented following the use of *Datura stramonium* and other varieties of Datura.

The experiences induced by Datura are usually unpleasant as well as dangerous.

The use of this type of plant is totally advised against for these reasons.

Note: Burundanga

Burundanga is a Datura preparation that has become popular as a chemical submission drug to perpetrate crimes such as robbery or sexual assaults. In fact it is considered a "date-rape drug". However, a prospective study in Barcelona did not find any of the drugs classically considered "date-rape drugs" (such as flunitrazepam, GHB, ketamine or scopolamine) in the analyses, alcohol being the main drug (which was mentioned by each and every one of the people in the group with suspected chemical submission drugging), followed by other psychoactive substances, mostly stimulant drugs.

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KRATOM

KRATOM

Kratom is a tree whose leaves contain alkaloids such as mitraginine, with both stimulating and sedative effects, depending on the dose. It has been used to increase physical performance and as a substitute for opiates.

BASIC INFO

Kratom is a tree native to the tropical forests of Southeast Asia. Its leaves have been used since antiquity for its intoxicating, stimulating and medicinal properties. The active principle of Kratom is mitragynine, although it contains a high quantity of alkaloids.

Low doses of Kratom appear to have stimulant effects, while higher doses have sedative effects.

It has recently been marketed in the West as a recreational substance, as well as for its properties that relieve symptoms of opioid withdrawal syndrome. It is sometimes used as a substitute for opiates.

The use of Kratom entails some physical risks that must be taken into account, particularly interactions with other substances and its ability to produce dependence.

ORIGIN / HISTORY

Kratom (*Mitragyna speciosa*) is a tree of the Rubiaceae family, native to the tropical forests of Southeast Asia, the Philippines and New Guinea, which can reach 4-16 meters in height.

It is known by different names in different places: Kratom, biak or ketum in Malaysia, krathom or thom in Thailand.

TRADITIONAL USES

There is a long tradition of using Kratom leaves for different purposes.

In some places in Southeast Asia (northern Malaysia and southern Thailand) Kratom leaves have been used since ancient times, both chewed and as infusions, for their stimulating effects by local rubber workers and fishermen to combat fatigue and increase productivity.

It has also been used for centuries for its medicinal properties to treat different conditions, in particular addiction to morphine, as well as being a substitute for opium in times of scarcity. Rural people in Malaysia and Thailand have traditionally used Kratom to treat diabetes, diarrhea, fevers and pains, and as a poultice to heal wounds. In these communities, Kratom is considered a better alternative to other illegal drugs and there is no social stigma associated with its use. Traditional Kratom users do not appear to have greater risk behaviors or difficulties adapting to their social environment, although Kratom's ability to produce addiction has been observed.

In addition to these uses, Kratom is also consumed socially at gatherings and celebrations.

USES IN THE WEST

Recently, Kratom and its derivative compounds have appeared as recreational use products. Some *smart shops* sell different formulations of Kratom, such as capsules, sheets, lozenges, powders and concentrated extracts, which have often not been analyzed or their had their contents verified.

KRATOM

CHEMICAL COMPOSITION AND DOSAGE

The leaves of the Kratom tree contain more than 40 different alkaloids. The composition and pharmacology of Kratom is complex and has not yet been sufficiently studied. The major alkaloids responsible for the psychoactive effects of Kratom are mitragynine and 7-hydroxymitragynine.

The concentration of mitragynine in the dry leaves of trees originating in Thailand is 66%, while in Malaysian trees it is 12%. The proportion and concentration of alkaloids can vary greatly depending on the maturity of the plant and the variety.

Commercial products sold as Kratom usually contain a wide variety of phytochemical components, and concentrations in alkaloids can be highly variable. They usually contain a mixture of Kratom powder and added extracts. Different varieties of Kratom are often found on the market, associated with the color of leaf streaks: red, green or white. It is believed that different varieties have different effects in terms of stimulation, mood alteration or analgesia.

As for the doses, usually one to three leaves are chewed to feel the effects, although people accustomed to its use can chew several times in one day. A dry leaf of Kratom usually weighs about 1.7 grams, meaning that the usual doses are between 1 and 5 grams, although they depend on the potency of each particular plant.

Dosage of dry leaves:

» Low dose: 1-2 grams
» Average dose: 2 - 4 grams
» High dose: >5 grams

EFFECTS

Kratom has different effects, both stimulant and sedative, depending on the dose. Low doses tend to produce stimulant effects similar to those of caffeine, cocaine or amphetamines, while high doses are often associated with sedative or narcotic effects, which bear some resemblance to the effect of opiates.

At low doses users report the following effects:

» Feeling of greater alertness
» Greater physical energy
» Euphoria and wellbeing
» Greater empathy
» Greater ease of physical work
» Sexual Excitement (occasionally)

At high doses, the following effects have been described:

» Sedation
» Analgesia
» Less sensitivity to physical and/or emotional pain
» Calm
» Pleasant sensations
» Increased empathy

As for the adverse effects due to the use of Kratom, it is necessary to distinguish those that occur in the short term from those that are due to continued use over time. The most common adverse effects are described below, and a more detailed analysis can be found in the section on Health and Risk Reduction.

Unwanted effects:

» Increased anxiety, or nervousness.
» Nausea
» Constipation
» Difficulty sleeping
» Temporary erectile dysfunction
» Itchiness
» Excessive sweating
» Tolerance
» Need to consume more frequently than desired (addiction)

LEGAL STATUS

The Kratom plant, *Mitragyna speciosa* and/or mitragynine and/or 7-hydroxymitragynine are currently only controlled in a few European Union countries: Denmark, Latvia, Lithuania, Poland, Romania and Sweden. Kratom is also not controlled in the United States, although some states have specific regulations.

There has been regulation in countries to which Kratom

is native. In Thailand, the possession of Kratom leaves has been illegal since 1943, while Malaysia and Myanmar have also declared Kratom a controlled substance, as in Australia and Bhutan.

PREVALENCE OF USE

The use of Kratom in the West as a recreational substance is relatively recent, so there is not much data on the prevalence of its use.

Data from the EMCDDA report usage rates for those who have ever tried Kratom in their lifetime at 2.32% of the population aged 12-65 years in Thailand, according to a 2007 survey. Kratom is the most commonly used illicit substance in Thailand. In Europe, Kratom is a relatively common "legal high" on offer, and there are many online suppliers that provide Kratom as one of their main products, behind *Salvia divinorum*.

According to data from the 2017 Global Drug Survey, 2.4% of the 115,000 respondents had ever consumed Kratom in their lifetime, with 1.5% in the last year.

A 2016 study based on a survey of 8049 people in the United States shows that Kratom users are mainly middle-aged (31-50 year old) middle-income people who use it for the primary purpose of reducing pain (68%), to treat emotional or mental issues (66%) and as a treatment to alleviate withdrawal symptoms associated with prescription opioids.

HEALTH AND RISK REDUCTION

There is evidence that highlights the risks of using Kratom. The consumption of Kratom leaves or preparations can cause undesired effects, some of them potentially serious.

Some of these effects seem to be related to the habitual use of Kratom, and others are derived from the addictive potential and the withdrawal syndrome that can cause.

The most common adverse effects after prolonged use may include: anorexia, tremors, hyperpigmentation, weight loss, hair loss and addiction.

As for the potential addictive effects of Kratom, users report developing a tolerance to its effects (need to consume more to achieve the same effects) as well as a cross tolerance with opiates. The cessation of Kratom use can lead to withdrawal syndrome, which manifests itself with the following symptoms:

» Muscle pains
» Irritability
» Insomnia
» Mood swings
» Runny nose
» Diarrhea
» Muscle tremors

Kratom is sold as a substance for pain management and opiate withdrawal syndrome, as well as for its anti-depressant and anti-anxiety effects, which is why many people use it to self-medicate and as an opiate substitute. It is important for people who use Kratom to inform their doctor if they are prescribed pain medications that may create a cross-tolerance with Kratom.

Less common side effects include:

» Seizures (in high doses or in combination with other substances)
» Intrahepatic cholestasis
» Psychotic symptoms
» Acute respiratory distress syndrome
» Hypothyroidism

In the United States there were 660 calls to poison centers between 2010 and 2015 related to Kratom use. Of these calls, 24.5% had minor symptoms with no risk to the life of the patient and without subsequent consequences and were resolved quickly. 41.7% were of moderate severity, did not present a risk to life nor did they have any subsequent consequences, but did require medical intervention. 7.4% were severe, presented life-threatening symptoms and implied later consequences for users.

INTERACTIONS AND FATAL RISKS

There is evidence that the combination of Kratom with other compounds can be dangerous and even deadly. This is the case with the product called "Krypton" to which 9 deaths are attributed in Sweden. This compound contained Kratom and another substance called O-Desmethyltramadol, an analgesic opioid. The presence of this same compound has been documented in other products available on the internet.

In another case, the death of a user appears to be due to the combination of Kratom and propylhexedrine, an amphetamine-type stimulant, which is used in nasal decongestants.

The combination of Kratom with benzodiazepines and cold medications has been linked with the death of another user. Further, the combination of Kratom with the following substances has been associated with deaths: venlafaxine, diphenhydramine, mirtazapine; zopiclone, citalopram and lamotrigine.

These combinations should be avoided.

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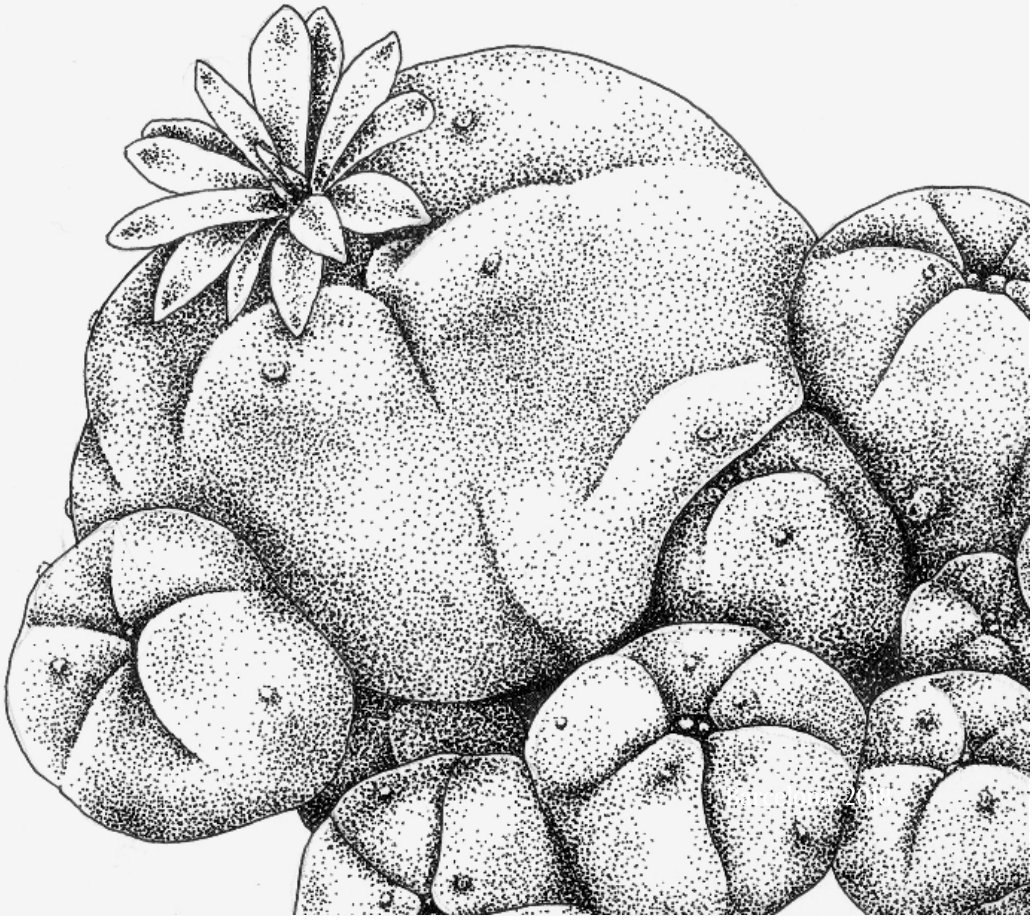
PEYOTE



PEYOTE

Peyote is a spineless cactus from the deserts of Mexico and the United States that contains mescaline. Since ancient times, different native peoples of North America and Mesoamerica have traditionally utilized peyote for medical and religious purposes.

BASIC INFO

Peyote, or *Lophophora williamsii*, is a spineless cactus that grows mainly in the deserts of northern Mexico and the southwestern United States of America. It commonly grows under bushes, and usually appears in groups ranging from three to more than fifty. Its growth is very slow and reaching maturity can take up to 15 or 20 years.

Peyote's area of distribution falls inside an irregular diamond that goes from Deming, New Mexico, to Corpus Christi, Texas, Sombrerete, Zacatecas and back to Deming. The zone that encompasses this diamond is the Rio Grande valley to the north, the mountains of Tamaulipas to the east, the basin of the tributaries of the right bank of Rio Grande de Santiago and the Mezquital river to the south and the foothills of the Sierra Madre, the Sierra de Durango and the Sierra de Nayarit. It usually grows in calcareous or chalky, clay soils from the Cretaceous formation north of this region.

Its shape and size is variable, some with circular shapes reaching up to 20 centimeters in diameter. There are other shapes that are similar to a carrot or a turnip, but without leaves or branches. It is divided radially by grooves that can be straight, slightly spiral, sinuous, or more complicated shapes that form "buttons". These buttons have small tufts of thick grayish white hair. The name of peyote's modern botanical classification, *Lophophora,* is due to this characteristic, which means "I have tufts". In the center of its upper part there is a small point of very thick fuzz, where a light pink flower appears at certain times of the year.

It is known by many names among which the following stand out: peyote, piote, hikuli, hikuri, devil root, challote, cactus pudding, mescal button, peote, earth cactus and whiskey cactus.

ORIGIN/HISTORY

The use of peyote in Pre-Columbian America

Anthropological evidence found in South Texas and in certain places in Mexico suggests that the practices and/or rituals in which peyote was used by native peoples of these zones may have an approximate age of up to 5700 years. Recent studies through carbon-testing have dated the age of dried peyote buttons found in cave number 5 of Shumla, Rio Grande, Texas and the buttons turned out to be between 3780 and 3660 BCE. These buttons still contained 2% mescaline, making them the oldest psychoactive botanical sample ever found.

During the time of the Spanish occupation, certain missionaries described practices related to this cactus. Fray Bernardino de Sahagún, for example, wrote in 1560 about certain peoples - Toltecs and Chichimecas - who had been using peyote since 1890 years prior to the arrival of the Spaniards to the territory they inhabited, according to indigenous narratives.

There is no general agreement about which people were the first to use peyote, some authors suggest that it was the Tarahumara, others claim that it was the Chichimeca people to first discover its psychoactive properties - both indigenous peoples of northern Mexico. Later this knowledge was shared with the Coras, Huicholes, Tepehuanos and Mexicaneros, among others.

The ethnologist Carl Lumholtz estimates that the use of peyote actually dates back more than three thousand years, since a symbol used by the Tarahumara in peyote ceremony appears in ritual carvings dating from that era and since preserved in volcanic rocks.

PEYOTE

Traditional contemporary use of peyote

Peyote is considered sacred among different native peoples of Mexico such as the Wixarika (Huicholes), Nayeeris (Coras), O'dham (Tepehuanos), Raramuris (Tarahumara), Yaquis, Yoemes (Mayos), Purépechas and Chichimecas. Also in the southern United States by people such as the Sioux or Lakota, Cherokee, Apaches, Dinè (Navajos), among others. Most of these people live in the deserted cultural area defined as Aridoamérica, an arid zone north of Mesoamerica.

There are more than 40 nations of American Indians in many parts of the United States and Canada who use peyote as a religious sacrament. Their tradition is younger compared to certain Mexican tribes, mainly the Wixarikas, Coras and Tarahumara. The contact between these different peoples originated mainly from commercial and familiar relations between them and it seems that the first native North Americans who learned to use peyote were the Kiowas and Comanches during their visits to indigenous groups in northern Mexico.

One of the most important figures in the expansion of the use of peyote in modern times was John Wilson, who developed a ceremony called "Great Moon" and was responsible for bringing this knowledge to most of the northern tribes of North America. In contrast to these ceremonies, a tribal chief named Elk Hair developed the "Little Moon" ceremonies, which entirely eliminated the Christian imposition on the rite and recognized First Nation Indians as the only ones who could celebrate these ceremonies.

Today the Native American Church (NAC) continues with the rites initiated by John Wilson. In this Christian-influenced church peyote is used as a sacrament and has about 250,000 followers. Members of the NAC are allowed to use peyote under the United States Indigenous Religious Freedom Act.

In Mexico, the worldview of the Wixarika, also known as the Huichol, is intimately related to peyote. The life of this indigenous people revolves around a calendar that includes offerings, pilgrimages, festivals and celebrations related to the knowledge bestowed by peyote. Among the variety of nations that consume peyote, the Wixarika are considered its guardians, given that their tradition of using the cactus is older.

One of the most well-known and important rites of the Wixarika peyote cult is the pilgrimage to Wirikuta in the desert of San Luis de Potosí, sacred place of the Huichol people as well as certain other groups. This pilgrimage is the most sacred act within their festive calendar, since it is when the peyote collection that will provide for the celebrations for the rest of the year occurs. The Wixarikas traditionally travel on foot, although today the pilgrimage of more than 400km that separate them from Wirikuta is made by bus and vans.

Peyote and mescaline were the first psychedelic substances to which Westerners had access, and for this reason they are probably the substances that have had the greatest presence in Western literature. Mescaline was the first psychedelic substance synthesized in its pure form. Aldous Huxley wrote about it in 1954 and popularized its effects in "The Doors of Perception". The books of Carlos Castaneda also popularized interest in peyote. Mescaline was also the first psychedelic substance that aroused the interest of scientists.

CHEMICAL COMPOSITION AND DOSAGE

In 1888 Louis Lewin published the first chemical study on peyote - the first time that an article about a psychoactive plant in the West was published. He isolated an alkaloid he called anhalonine, which today is considered to be a mixture of various alkaloids. Years later, between 1895 and 1896, Arthur Heffter published two more studies on peyote, in which he described having isolated four different alkaloids: mescaline, peyotine, anhalondinine and lophophorine. Heffter also performed self-tests to find the psychoactive action of these alkaloids and discovered that isolated mescaline had effects almost indistinguishable from peyote. In 1919 Mescaline was identified as 3,4,5-Trimethoxy-B-Phenethylamine, and thus became the second psychoactive alkaloid isolated from a plant. The first was harmine of *Peganum harmala*.

Subsequently more than 50 different alkaloids have been

PEYOTE

isolated in the peyote plant, and the alkaloid content is around 8% of the dry plant weight.

Mescaline is a phenylethylamine, a class of substances that share a similar structure. Other substances in this group are amphetamines, such as MDA or MDMA, catecholamines, such as the neurotransmitters dopamine and adrenaline and many medications - antidepressants, bronchodilators, etc.

Regarding the dosage of the plant, in ceremonial contexts, 30 to 150 grams of dry and pulverized peyote per person are usually ingested. The amount in buttons is usually four to twelve peyote buttons, although in certain ceremonies participants may consume more throughout the night. Sometimes an infusion of peyote is prepared, and after blending the buttons, the equally bitter liquid containing the alkaloids is consumed.

Dosage of mescaline

The active dose of oral mescaline hydrochloride is between 150 and 700 milligrams. The usual doses of mescaline have been calculated based on 3.75mg of mescaline per kilogram of body weight.

» Threshold dose: 100mg
» Low dose: 100-200mg
» Average dose: 200-300mg
» High dose: 300-500mg
» Very high dose: 500-700mg

EFFECTS

The first written documentation of peyote in detailed form were those of Fray Bernardino de Sahagún, who reported frightful visions, laughing, the urge to fight, courage, protection from dangers; besides being a resource used in times of thirst or hunger.

Peyote has a bitter and pungent taste, and usually induces nausea and more rarely vomiting. Synthetic mescaline also produces nausea and vomiting, although to a lesser extent, so it seems that the effect is not only due to the other alkaloids present in the plant but an effect of mescaline itself.

The effects of peyote take some time to present. This period of onset of the effects can last from 2 to 4 hours. The experience is later sustained for about 6 more hours before gradually declining. The total duration of the experience is usually around 10-14 hours.

The effects induced by peyote, and its main psychoactive alkaloid, mescaline, belong to the group of so-called "classical psychedelic" effects, together with LSD, psilocybin mushrooms (psilocybin), ayahuasca and DMT. Peyote shares the ability to induce profound changes in perception, consciousness and cognition with this group of substances. Visions can appear with eyes open and closed, an increase in sensory perceptions - brighter colors, sound is perceived in greater depth - as well as experiences of psychological insight and transcendent and spiritual experiences and changes in the perception of space, time and one's self-image.

Peyote is slightly more stimulating than psilocybin mushrooms or ayahuasca. Since mescaline belongs to the phenylethylamine group and its structure is similar to other psychoactive substances such as amphetamine or MDMA, it shares some of the stimulant effects of these, although to a lesser extent. It has not been reported that mescaline or peyote have addictive potential, and in fact some communities of the Native American Church use peyote to treat problems of addiction to alcohol and other substances.

PREVALENCE OF USE

Peyote and mescaline, although a relatively well-known substance due to publicity in the 1950's-70's, is still a substance very infrequently consumed in Western society. In results from the Global Drug Survey of 2017, it is not even listed among the 40 substances surveyed. In previous decades some people believed they had used mescaline, although in many cases, according to some authors, it was probably LSD. The dose of mescaline is relatively high compared to other substances sold on the

illicit market, its synthesis or extraction is expensive and difficult, with the result that synthetic mescaline is not usually found on the black market. Peyote is a protected and slow-growing species, and one must ingest a substantial amount of buttons to experience psychoactive effects. Therefore, the prevalence of consumption of peyote and mescaline is considerably low compared to other substances.

As for people who consume peyote in ceremonial contexts, it is estimated that the Native American Church has around 250,000 members in Mexico, the United States and Canada. The members of this church usually use peyote with some regularity. According to data from 2003, the Huichol population comprises only about 44,000 people.

LEGAL STATUS

The psychoactive alkaloid of peyote, mescaline, is a substance controlled by the 1971 Vienna Convention and is included as Schedule I. It is therefore considered a substance whose use, sale and manufacture is prohibited. However, the peyote cacti is not included on the lists of the conventions, and its regulation depends on the legislation of each country. Thus, in Canada mescaline is classified as Schedule III, and peyote is explicitly exempt from regulation if it is not prepared for ingestion, while in Brazil, France, Italy and other countries peyote is considered illegal. Other countries, such as Spain, do not mention peyote on their lists of controlled plants, although this does not mean that the sale of peyote can not be considered an illegal act.

In the case of US legislation, the use of peyote is only allowed in ceremonial contexts for people belonging to the Native American Church.

The Mexican government was one of the countries that, upon joining the 1971 agreement and ratifying it on February 20, 1975, made an express reservation with respect to its application. Certain indigenous ethnic groups that traditionally use wild plants containing psychotropic substances among those listed as Schedule I, peyote being among them, exist in Mexico's territory. Thus, the peyote cactus is not strictly prohibited or regulated, since it is not included in any section of the General Health Law and its use is allowed by the Huichols. Even so, peyote is considered an endangered plant, so its collection is prohibited, except in cases of traditional use by indigenous peoples.

HEALTH AND RISK REDUCTION

Physical Health

Due to the possibility of intense experiences that generate anxiety, people with a history of cardiovascular diseases, particularly those who are taking medication to control these pathologies and who have reduced physical activity due to medical advice should refrain from using peyote.

Peyote has slightly stimulating effects, so it should not be combined with other stimulating substances.

Psychological health

As with any psychedelic substance, it is extremely important to consider three factors when it comes to reducing the risks associated with its use: the dose, the set, or one's prior mental state, and the setting, meaning the context in which it is used.

Regarding the dose it is important to know that the effects of mescaline and peyote can take up to two hours to appear, so one can make the mistake of believing that a dose was insufficient, re-administer and wind up taking a dose that is too high. It is important to calculate the dose in advance and wait for a sufficient amount of time before deciding to increase the dose.

As with any classical psychedelic, the effects of mescaline and peyote depend to a large extent on the mental state of the person taking it. Some researchers have called psychedelics "nonspecific amplifiers of consciousness", so their effects can be vastly variable from person to person, as well as on different occasions. Therefore, it is necessary to be cautious when using peyote in situations of stress, depression, worries or crucial difficulties.

In addition, the effects depend on the context in which these substances are used, as well as the company and the physical environment. For this reason, it is important to plan the way in which the peyote is going to be used appropriately.

People with a history of psychiatric conditions such as psychotic disorders, bipolar disorder, suicidal thoughts and others should refrain from using mescaline if it is not in a clinical context, as there is a risk of increased symptoms and decompensation.

As with any psychedelic substance, unconscious material may emerge during the peyote experience. These experiences can be emotionally intense and sometimes involve feelings of fear, anguish and difficulty, in the same way that they can cause experiences of joy and ecstasy. For this reason, it is usually recommended to have an open and accepting attitude towards the actual content of the experience.

Studies conducted among the Native American population and members of peyote churches have evaluated the cognitive performance and the psychological state of people who have consumed peyote for years in these contexts. The results indicate that there is no evidence of psychological or cognitive deficits among those who have used peyote in the Native American Church for extended periods. These results, although interesting, can not be extrapolated to other contexts and forms of use.

FORMS OF USE

In ancient times, people with knowledge of peyote used it for different purposes, among them the following: treatment of wounds, snake bites, bruises, rheumatism, dizziness, anxieties, toothache, hemorrhages, headache, phthisis, fever, chest ailments, and lung diseases in general. In addition, curative properties were attributed to peyote in the treatment of different mental conditions.

Peyote can be ingested fresh, dried and powdered, liquefied with water or mixed with chocolate or fruit.

Traditionally, the way in which it is consumed depends on the occasion and pertaining celebration. During the Huichol pilgrimage to Wirikuta, it is eaten fresh since it is consumed after its harvest; the lower part corresponding to the root is cleaned, and a thin, rough, dark brown layer is removed. Upon the return of the pilgrims, the other members of the community also eat fresh peyote at the welcome ceremony.

After concluding the pilgrimage, the peyote is dried and then ground to a powder. The powder can then be eaten in tablespoons or combined with chocolate or fruit.

In Native American Church ceremonies the peyote is pulverized or the buttons are placed in water, left to infuse, and then consumed in liquid during ceremonies that last all night.

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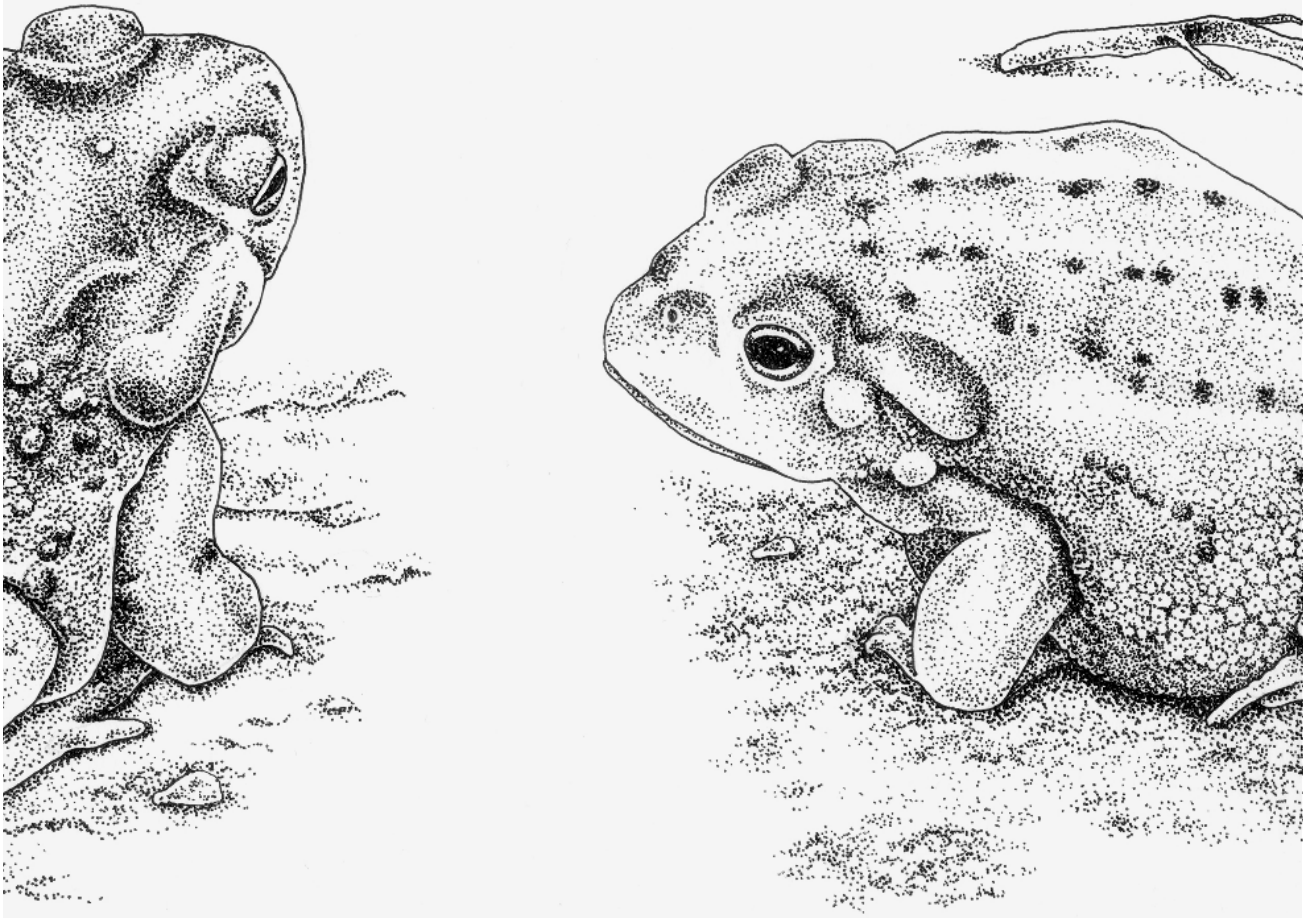
BUFO ALVARIUS



BUFO ALVARIUS

The psychoactive effects of the secretions of different varieties of toads have been known for centuries. *Bufo alvarius* is a semi-aquatic amphibian that lives in the Sonoran desert of Mexico. Their cutaneous glands contain more than a dozen tryptamine compounds, including bufotenin and 5-MeO-DMT, two powerful psychedelic substances.

BASIC INFO

The *Bufo alvarius* toad, whose correct name is *Incilius alvarius*, is native to the American continent. It can be found in the southern part of the Arizona desert in the USA and throughout most of the Sonoran desert in Mexico, even reaching Guamúchil, Sinaloa. It's also known as the Colorado River toad, because it inhabits the areas surrounding this river in lower California, New Mexico, Mexico and southern Arizona.

It is found mostly in the lower parts of the Sonoran desert, at altitudes ranging from sea level to 1600m. In addition to the desert, *B. alvarius* inhabits pastures and oak forests, where it hides in rodent burrows.

As a nocturnal toad, during most of the months from September to April it stays underground in a state of hibernation. During the breeding season, which coincides with the rainy season, it becomes very active, especially at night, and hundreds of toads roam the desert.

B. alvarius have large parotid glands that secrete a viscous, milky-colored substance. It is this venom that contains psychoactive alkaloids.

ORIGIN/HISTORY

Toads have always played an important role in the myths, legends, religions, medical practices and healing arts of different peoples throughout the history of mankind.

We find representations of toads that go back thousands of years. Some authors have suggested that Neanderthals used toad venom for hunting, divination and as an intoxicant.

There are myths and traditions related to toads throughout history in different parts of the world such as China, Tibet, Nepal, as well as Bolivia and Europe. Myths about the use of toads in witchcraft during the Middle Ages are widespread.

Several anthropologists suggest that one toad variety, *Bufo marinus,* has been used in Mesoamerica since ancient times for its intoxicating properties. The hypothesis regarding the use of *Bufo marinus*, whose secretions, like those of other toads, mainly contain bufotenin, is based on the presence of many iconographic and mythological representations of toads in the Olmec, Mayan and Aztec cultures, dating from 2000 BCE. In the archaeological remains of the Olmec culture of San Lorenzo, Veracruz, Mexico, skeletal remains of Bufo species have been found dating from 1250-900 BCE. Aztec sculptures and representations place great emphasis on the parotid glands of the toads, which is where the psychoactive secretions are located.

According to accounts from the Anglo-Dominican friar Thomas Gage, the native Mayan Poloman people of Guatemala had the habit of adding both tobacco leaves and venomous toads to their fermented beverages to increase their potency.

There has, however, been great confusion about the varieties of toads that could have been used for different purposes, as well as which alkaloids present in the secretions of the toads were responsible for the effects. As already mentioned, there are dozens of tryptamine substances in the venoms of certain toads and while the psychoactive effects are usually attributed to bufotenin and 5-MeO-DMT, the contribution of each alkaloid to the final effect has not yet been fully clarified. Moreover, some alkaloids present in the secretions of the toads of

the *Bufo* genus can have cardiotoxic effects and be fatal, as certain reports of animals that have died after biting toads demonstrate.

Some anthropologists have suggested that it is unlikely that *B. marinus* was the toad used by Mesoamerican cultures for psychoactive purposes, due to the presence of bufotenin in their secretions, whose psychoactivity has been doubted in recent decades. It has been proposed that the species used was *B. alvarius*, whose secretions contain 5-MeO-DMT and whose morphology is practically indistinguishable from *B. marinus*. However, given the lack of sufficient chemical analysis, this assertion is only speculative.

Today some traditional practices of the use of psychoactive toads survive among healers of Mesoamerican and South American tribes, in which toad venom is used for magical purposes, mainly in the preparation of love potions and other uses.

While the importance of toads and their venoms in medical and religious practices and in the mythology of many ancient civilizations is indisputable, confusion remains about the varieties of toads used, as well as the modes of use and their purposes. Although possible, the traditional use of *B. alvarius* can not be assured.

CHEMICAL COMPOSITION AND DOSAGE

B. alvarius gland secretions contain different alkaloids from the indolealkylamines family and their metabolites from the more common series of 5-hydroxy-indolealkylamines, as well as 5-methoxy-indolealkylamines, unusual in the secretions of toads, known as bufotoxins.

Similarly to many other varieties of toads, *B. alvarius* produces bufotenin (5-OH-DMT) in considerable amounts, up to 3 mg per gram of dry skin. The skin of *B. alvarius* also contains other sulfurous substances, one of which is bufovidrine and other cardiotoxic substances called bufogenin and bufotoxin. Some studies have regarded bufotenin to be the substance responsible for the psychoactive effects of both plants and toads, while other studies have not found signs of psychoactivity, although they have found toxic effects on a physical level. Jonathan Ott found in his bioassays that bufotenin administered by different routes (vaporized, intranasal, oral, rectal and endovenous) did have psychoactive effects at doses similar to 5-MeO-DMT.

The peculiarity of *B. alvarius* is that its secretions are the only ones that contain 5-MeO-DMT, or 5-methoxy-N,N-dimethyltryptamine of all known toad species. This is because *B. alvarius* has a special enzyme, called O-methyl transferase, which converts bufotenin into 5-MeO-DMT, a very potent psychoactive substance with psychedelic effects. The content of the secretions can reach up to 5-15% of the total dry weight in the parotid glands, which results in a considerable amount of 5-MeO-DMT. A single toad can produce up to 75mg of this substance.

5-MeO-DMT is present in several botanical varieties, such as different species of Virola, Anadenanthera and Phalaris, plants that have been used in the preparation of psychoactive snuffs since ancient times. 5-MeO-DMT has also been found in human fluids including urine, blood and cerebrospinal fluid, so it seems that the human body can also synthesize this substance.

Bufotenin Dosage

Reports on psychoactivity and the effects of bufotenin have been controversial and different studies have drawn different conclusions. Therefore, the dosage of bufotenin and its specific effects are not clearly defined. According to Jonathan Ott's bioassays, the doses of bufotenin are the following:

Intranasal or sublingual

» Low dose: 20 - 30mg
» Average dose: 30 - 60mg
» High dose: 60 - 100mg

Oral

» Average dose: 100mg

Smoked/vaporized: the dosage is similar to that of smoked 5-MeO-DMT

» Low dose: 2mg
» Average dose: 4 - 8mg

Rectal (in suppository)

» Low dose: 30mg

Dosage of 5-MeO-DMT

5-MeO-DMT and the plants that contain it have traditionally been consumed by insufflation, or snorting, in mixtures of plants known as snuffs. The dosage of pure substance via insufflation is the following:

» Threshold dose: 3 - 5mg
» Low dose: 5 - 10mg
» Average dose: 8 - 15mg
» High dose: 10 - 25mg

The dosage of pure smoked substance is between 6 and 20 mg, and is currently the most commonly used route:

» Threshold dose: 1 - 2mg
» Low dose: 2 - 5mg
» Average dose: 5 - 10mg
» High dose: 10 - 20mg

The intravenous dosage has also been investigated, and it has been determined to be between 0.7 and 3.1mg.

There are reports of oral and sublingual doses of 5-MeO-DMT although the results are unclear. In these cases the doses are around 10mg sublingually, and 20-30mg orally. Sometimes 5-MeO-DMT is used as an additive in ayahuasca admixtures, usually due to the use of a plant that contains it. In combination with monoamine oxidase inhibitors, the oral effects can be much greater and involve significant risks, which will be mentioned later.

The effects of *B. alvarius* venom are not necessarily identical to those of pure 5-MeO-DMT. As has been mentioned, toad venom contains numerous substances and the role of each of them in the total effect is not known with any certainty. There are also no studies regarding the quantity of smoked toad secretions necessary to achieve psychoactive effects, although based on analyses suggesting that the secretions contain up to 15% alkaloids, it would require about 65mg of toad venom in order to obtain 10mg of 5-MeO-DMT.

EFFECTS

When smoked/vaporized, 5-MeO-DMT presents immediate and short effects, usually less than 20 minutes in duration, although of an often unexpected and overwhelming intensity.

When the vapors of 5-MeO-DMT are inhaled, the effects are established within a few seconds and their appearance is sudden and unexpected. The maximum effects begin in less than 1 minute and last for about 5-15 minutes. Users often describe the appearance and plateau of the effects as extremely intense. Afterwards the effects disappear quickly, after about 5-15 minutes, although most people feel residual effects for up to an hour after having smoked the substance.

Experience with *B. alvarius* venom is usually very immersive, and produces an extreme variation in perception. Many people describe sensations of cosmic unity, of access to non-dual consciousness and deep spiritual experiences. Some people have compared it to the experience of dying and accessing states similar to those described in Buddhist and Hindu traditions such as Nirvana or Tathāgata, beyond the beyond. The loss of a sense of identity and dissolution of the ego is common, as well as oceanic sensations of merging with everything.

Also, due to the rapid and intense onset of the effects, reactions of fear and panic are common, and the experience can be overwhelming and traumatic for some people. Movements can be produced during the experience, as well as involuntary expressions of sounds such as screaming, singing, or crying without the individual being aware of it.

Via insufflation (snorting), the effects tend to be more progressive and less overwhelming than from smoking,

although they can be equally intense. The total duration of the most prominent effects is around half an hour to one hour, with residual effects of up to three hours. The venom of *B. alvarius* is not usually used via insufflation due to its consistency; the snorted consumption of pure 5-MeO-DMT is somewhat more common.

LEGAL STATUS

B. alvarius is not on any list of controlled species. Neither 5-MeO-DMT nor bufotenin are on the psychotropic lists of the United Nations Convention on Psychotropic Substances of 1971. This means that in most countries they are not controlled substances, except for those in which there is separate legislation, such as in the United States of America, where both bufotenin and 5-MeO-DMT are classified as Schedule I, and therefore their sale, possession and use is illegal. Similarly, in the United Kingdom both substances are controlled as Class A. Other European countries, such as Sweden, have also included these substances on their lists of controlled substances.

HEALTH AND RISK REDUCTION

5-MeO-DMT, *B. alvarius* and the toxins they contain pose health risks that are important to consider.

Plants containing 5-MeO-DMT have not been used traditionally in combination with plants that contain beta-carbolines (harmine/harmaline) in preparations that are to be ingested orally. There are reports of combination of these substances in psychoactive rapés (snuffs) that have been inhaled and in smoked preparations.

The combination of 5-MeO-DMT, as well as bufotenin, with beta-carbolines ingested orally and the subsequent inhibiting effects of the MAO (monoamine oxidase) involves dangerous risks. This combination can produce hyperthermia, according to studies in animals, and this deregulation of the mechanisms responsible for controlling body temperature can have serious adverse effects.

There are reports of people who have died after combining beta-carbolines and 5-MeO-DMT orally, so this combination should be avoided and/or treated with great caution. In the case of combining ayahuasca and *B. alvarius*, it is advisable to wait 24 hours after using ayahuasca before inhaling the venom, to eliminate the inhibitory effects of the monoamine oxidase in the harmalines. In the case of first using *B. alvarius*, it is recommended to wait a minimum of one hour before taking ayahuasca. Regarding the risks of combining ayahuasca with *B. alvarius*, see:

http://news.iceers.org/es/2017/05/alerta-bufo-alvarius-con-ayahuasca/

An experience with *B. alvarius*/5-MeO-DMT can be overwhelming and immersive, to the point of losing external references and even controlling one's body for some minutes. Some people move during the experience in an unpredictable way. Therefore the presence of a sober caregiver who can maintain the physical safety of the individual and the environment is highly recommended, that is to say, necessary.

The psychological risks of an experience with *B. alvarius* also have to be taken into account. The experience can be very pleasant and transcendent, but it can also be frightening and traumatic. Taking into account the factors of the setting, one's previous mental state and expectations, as well as the person who administers the substance is important when deciding on the use of *B. alvarius*. Some people report re-experiencing the effects after the event, particularly during subsequent evenings.

Unlike other psychedelic substances, *B. alvarius* induces an experience in which one can lose awareness of being under the effects of a substance, and even lose one's consciousness of oneself and of the environment. This disappearance of self-consciousness, or the death/dissolution of the ego, are experiences that are difficult to explain, and over which it is difficult to maintain any sense of control. Those who consider experimenting with this substance should take this into account before doing so and know that the experience can be both revealing and blissful, as well as terrifying.

BUFO ALVARIUS

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PSILOCYBIN MUSHROOMS

PSILOCYBIN MUSHROOMS

In Nahuatl, the language of the Aztecs, the name for psilocybin mushrooms is Teonanácatl, which has been translated to "flesh of the gods". There are more than 180 varieties of mushrooms that contain psilocybin and psilocin, the alkaloids responsible for their psychoactive effects. They are popularly called "magic mushrooms" and are perhaps the best known psychoactive plant variety.

BASIC INFO

The different varieties of psychoactive mushrooms, also known as magic mushrooms, which contain psychoactive alkaloids such as psilocin, psilocybin and baeocystin, belong to the families Strophariaceae and Hymenogastraceae of basidiomycete mushrooms, of the Agaricales order. The most common and well-known genera that produce species that contain these alkaloids are *Psilocibe* and *Panaeolus*.

Some of the best known species are the *Psilocybe semilanceata, Psilocybe cyanescens, Psilocybe azurescens* and, above all, the *Psilocybe cubensis*, of which there are dozens of varieties such as the B+, Ecuador, Mazatapec, and many many more.

Psilocybin mushrooms have been used by different cultures for their intoxicating effects, particularly in the Mesoamerican Aztec peoples of the pre-Columbian era and later among the Mazatecs and Zapotecs.

ORIGIN/HISTORY

There are more than 180 species of mushrooms that contain tryptamine alkaloids such as psilocybin and psilocin. They include the genera *Psilocybe* (117 species), *Gymnopilus* (13 species), *Panaeolus* (7 species), *Copelandia* (12 species), *Hypholoma* (6 species), *Pluteus* (6 species), *Inocybe* (6 species), *Cnocybe* (4 species) and *Agrocybe*, *Galerina* and *Mycena*.

The genus *Psilocybe* is the most common, and most of its species are found in humid subtropical forests. Mexico is the country where the greatest variety of psychoactive mushrooms can be found.

Although psychoactive mushrooms are found from Alaska to southern Chile, Australia and New Zealand, Hawaii, Europe, Siberia, Japan and Southeast Asia, precise knowledge of their geographical distribution is not well established.

Different varieties of magic mushrooms have been used by people around the world since ancient times. Indigenous groups have revered the visions induced by mushrooms, and have used them in their magico-religious rituals to communicate with the spiritual world, the spirits of the deceased and to obtain knowledge and healing.

The oldest samples of the probable use of mushrooms, although not totally conclusive, can be found in a mural in Tassili, in the Sahara desert, southeast of Algeria. In this mural, which dates from between 7000 and 9000 BCE, mushrooms as well as anthropomorphic figures carrying mushrooms are represented. As for what type of mushroom is depicted, some authors have speculated that it is *Psilocybe mairei*, a known species of Algeria and Morocco. Others, however, doubt the authenticity of these paintings.

In the Selva Pascuala mural, in Cuenca, Spain, dating from the Upper Paleolithic (6000 BCE) to the Middle Neolithic (4000 BCE) eras, one can find representations of mushrooms, which have been identified as *Psilocybe hispanica* and *Psilocybe semilanceata*. In these murals figures of bulls are represented, so some authors correlate the relationship of fungal growth with the habitat, since these species grow in bovine feces.

We also find the use of psychoactive mushrooms in Asia. In Japan we have the *Gymnopilus spectabilis*, also known as maitake or "mushroom dancer", whose use was compiled by Minamoto Takakuni in a book of tales, the Konjaku Monogatari, dating from the late 9th century CE. This mushroom has also been known as owaraitake or "laughter mushroom". Parietal pictorial representations have

also been found in caves and shelters in South Africa and Australia, among other places.

In the New World different groups have used and continue to use psilocybin mushrooms. In particular, different Mexican ethnic groups, such as the Mazatecs, Mixitecas and Zapotecs, among others. Vessels in the shape of mushrooms have been found associated with the pre-classical and classical Mayan periods in Mexico, Guatemala, Honduras and El Salvador, dating from between 500 BCE and 900 CE and suggesting ancestral knowledge of the use of psilocybin mushrooms. The first documented reports about the use of mushrooms are from an indigenous person named Tezozomoc, who wrote in Spanish in 1598 about the use of intoxicating mushrooms in the celebration of the coronation of Moctezuma II in 1502, during the Aztec civilization.

There are representations of mushrooms in Mexican art that survived the conquest. Good examples of this are the Codex Vindobonensis, the Codex Magliabechiano, and the famous frescoes of Tepantitla, in the city of Teotihuacan.

Reports by Spanish colonizers, such as one from Fray Bernardino de Sahagún, called "A General History of Things in New Spain", described the use of mushrooms not only in celebrations but also in religious, medical and divination ceremonies. Sahagún's writings describe the use of the name teunamacatlh (teonanácatl) to denote psilocybin mushrooms. Teonanácatl has been translated as "flesh of the gods", although other authors suggest that "sacred mushrooms" or "marvelous mushrooms" would be more literal translations.

The Spaniards believed that the use of the mushroom was contrary to Christian morality, and in 1620 the tribunal of the Inquisition declared its use heretical, as well as that of any other intoxicating plant, and harshly repressed healers and those who ingested the mushroom. Henceforth, the traditional use of psilocybin mushrooms was relegated to clandestine secrecy.

The rediscovery of the traditional use of psilocybin mushrooms in the New World occurred thanks to the work of Reko and Schultes, who obtained and identified three different varieties of visionary mushrooms in Huautla de Jiménez, Oaxaca, in 1938. That same year, Irmgard Weitlaner and Jean Basett Johnson attended a mushroom ceremony, although they did not ingest any and therefore did not experience its effects.

In 1952, Gordon Wasson and his wife Valentina Pavlovna began to take an interest in the psilocybin mushroom cult, and after a review of the available documents and contacting Schultes, Reko, Johnson and Weitlaner, they began their trips to Huautla de Jiménez. During the summer of 1955, Gordon Wasson and his photographer Allan Richardson attended a psilocybin mushroom vigil with Maria Sabina - a Mazatec shaman - and were the first Westerners to experience and report the effects of mushrooms and their traditional uses among Mazatecs.

CHEMICAL COMPOSITION AND DOSAGE

The active principles present in psilocybin mushrooms are psilocybin (4-PO-DMT), psilocin (4-HO-DMT) and baeocystin (4-HO-NMT). Psilocybin is the main component of most varieties and the most stable alkaloid of the three.

Psilocybin was isolated by the Swiss chemist Albert Hofmann in 1957, from Psilocybe mexicana mushrooms, cultivated in Paris by the mycologist Roger Heim from mushrooms collected in Mexico during Heim and Wasson's expedition. Hofmann is known to have synthesized LSD (lysergic acid diethylamide), and was also the first to synthesize psilocybin in 1958.

Studies on the pharmacology of psilocybin indicate that psilocybin is converted to psilocin once absorbed, and that equivalent amounts of psilocin produce the same subjective effects as psilocybin. Therefore psilocybin is sometimes considered a stable precursor, or prodrug, but the psychoactive alkaloid responsible for the effects of mushrooms is psilocin.

There are no specific studies and there is very little information on the effects and pharmacology of baeocystin.

The potency of psilocybin mushrooms varies great-

ly depending on the species and variety, as well as the conditions in which they have grown and the age of the mushrooms.

Common varieties such as *Psilocybe cubensis* and *Psilocybe semilanceata* contain around 6 -10mg of psilocybin per gram of dried mushrooms. Other varieties, such as *Psilocybe azurenscens* and *Psilocybe bohemica* contain a higher amount of psilocybin, around 1.78% and 1.74%, respectively.

There are varieties of intermediate potencies, such as the *Panaeolus cyanescens*, also known as *Copelandia cyanescens*, which contain 0.85% psilocybin.

Dosages of **pure psilocybin** are as follows:

» Microdose: < 4mg
» Low dose: 4 - 8mg
» Average dose: 6 - 20mg
» High dose: 20 - 35mg
» Very high dose: > 35mg

Dosages of mushrooms vary depending on the species, its state of preservation, if they are fresh or dried mushrooms and other factors, so adjusting the doses of mushrooms is always imprecise. Usually the doses for usual varieties (*P. cubensis* and the like) of **dry mushrooms** are as follows:

» Microdose: < 0.25gr
» Low dose: 0.25 -1gr
» Average dose: 1 - 2.5gr
» High dose: 2.5 - 5gr
» Very high dose: > 5gr

EFFECTS

Psilocybin mushrooms produce psychoactive effects in humans very similar to the rest of the classical psychedelics such as LSD and mescaline. Most users describe the experience as an internal journey, in which they go through different phases with varying effects. The first effects usually begin to be perceived earlier than with LSD or mescaline, and by about 30 minutes after ingestion they can be discerned. The maximum effects are usually established between 60 and 90 minutes after ingestion, and they last for about two hours before starting to diminish. The total duration of the experience is around 4 to 6 hours, depending on the dose.

Physical effects

Physically, the main effects of psilocybin include dilation of the pupils and slight increases in blood pressure and heart rate, especially at high doses. Variation in blood pressure seems more related to subjective experience than to the physiological effects of psilocybin, particularly if anxiety appears. Nausea can sometimes occur, especially when mushrooms are ingested rather than pure psilocybin, and more rarely vomiting or diarrhea. Tremors, muscle discomfort and dizziness may also occur.

The physical effects in general are usually mild and not significant.

Psychological effects

Psychological effects are characterized by marked alterations of sensory perceptions as well as profound changes in consciousness and cognition.

At the sensory level, visual alterations may occur in the form of colorful kaleidoscopic visions with closed eyes, intensification of colors, distortion of the shapes of objects or surfaces that undulate or move. Auditory disturbances may also appear, such as an increased appreciation of music and sounds. Synesthetic experiences can occur, in which stimuli corresponding to a certain sensory field are perceived and processed by another sense; for example, sounds that are perceived as visions. The sense of touch can also be altered, experiencing an increase in tactile sensitivity, sensations of cold or heat, tingling or a feeling of energy running through the body, as well as paresthesia.

At the cognitive and consciousness level, these alterations can be very intense and seem to be experiences as positive as they are terrifying.

Recent studies have observed the ability of psilocybin to induce mystical experiences in controlled contexts and in

high doses. These mystical experiences include feelings of numinousness, profoundly positive emotional states, internal unity, transcendence of time and space, ineffability and a sense of unity and interconnection with all things.

Frightening experiences may include sensations of agonizing fear, paranoia, a sense of dying or going crazy, feelings of depression or anger, high anxiety, agitation, confusion, and disorientation both spatiotemporally and internally. This phenomenon has sometimes been called a "bad trip". Only rarely are psychotic symptoms produced, which usually disappear when the effects subside.

In most cases, however, the experiences induced by mushrooms contain both positive and pleasant elements, as well as less pleasant components that could be experienced as psychologically challenging. Experiences in which personal biographical material emerges are common, as well as content related to significant others. In addition, there may be a dissolution of personal limits, or a dissolution of the ego, with sensations described as "oceanic", which can be perceived as a transcendent experience, but may also result in anxiety.

Some studies show that psilocybin produces an increase in positive mood, and a positive bias in the perception of stimuli, related to a possible decrease in the activity of the amygdala, the brain structure responsible for the processing of potentially threatening emotions.

Effects in controlled contexts

In addition to the ability of psilocybin to induce mystical experiences, other potentially therapeutic effects have been found in clinical trials.

The use of psilocybin in the treatment of anxiety and the increase in quality of life in cases of people with advanced cancer diagnoses has been investigated. Psilocybin has also been used in research for the treatment of cluster headaches as well as obsessive-compulsive disorder. Studies on the use of psilocybin in tobacco and alcohol addiction have also been undertaken. Research is currently being conducted on the therapeutic potential of psilocybin for treatment-resistant depressive disorders with promising results.

LEGAL STATUS

The active ingredients of psilocybin mushrooms, psilocybin and psilocin, are controlled substances on Schedule I of the 1971 United Nations convention. Therefore, the sale of these substances is illegal.

However, mushrooms containing these substances are controlled differently in particular countries, according to each country's interpretation of Schedule I. In Schedule I of the 1971 Convention, only active ingredients appear, not the natural materials that contain them (such as mushrooms or plants), which leaves the interpretation of the prohibition of botanical materials open to the particular laws of each country. Furthermore, in many countries these mushrooms grow wild.

In most European countries, psilocybin mushrooms are illegal and can not be bought or sold. The mode in which the mushrooms had been sold in recent decades was considered a "product" and/or "preparation" of psilocybin, so any presentation of said mushrooms was considered illegal.

For several years mushrooms were available for purchase and sale in smart-shops in the Netherlands. They could legally acquire fresh as well as dried mushrooms since they were legal until 2002. After that year, dried mushrooms were declared illegal, although they could continue selling fresh mushrooms. That situation changed and the sale of fresh mushrooms has been illegal since 2008. An exception is the Sclerotia variety, also known as "truffles" or "philosopher's stones", which can still be purchased, as it is not a mushroom, but mycelium.

Mushroom spores, as well as culture kits that do not contain mushrooms, and therefore their active ingredients, are sold in smart-shops in some countries.

PREVALENCE OF USE

The prevalence of mushroom consumption in the EU is considerably lower than that of cannabis, and it seems to be equal to the prevalence of ecstasy use (MDMA) in some countries among students aged 15-16 years. Surveys

in 12 European Union countries indicate that between 15 and 24 years of age, the use of psilocybin mushrooms at some point is between 1% and 8%. According to the published results of the 2017 Global Drug Survey, psilocybin mushrooms are the substance with the eighth highest consumption ever among the surveyed population behind alcohol, cannabis, tobacco, beverages with high caffeine content, pipe tobacco (shisha), MDMA, and cocaine. According to this survey, 24.4% of the respondents had consumed mushrooms at some time in their lives.

In this same survey, psilocybin mushrooms were the substance that had generated the least requests for emergency medical treatment; only 0.2% of people who used them requested medical attention. In this sense, mushrooms have been considered the safest substance reported. As for the occurrence of difficult experiences, mushrooms are the substance that caused the least difficult episodes of all psychedelic substances investigated, both of plant origin (ayahuasca and peyote) and synthetic (LSD, NBOMe, 2C-x, and smoked DMT) .

In some EU countries it is more common to consume mushrooms collected in their natural habitat, while in other countries users usually grow their own mushrooms. In Norway, Scotland, Switzerland, the United Kingdom and Denmark mushroom picking predominates, while in Belgium, Holland, Germany and Finland, self-cultivation is more common.

HEALTH AND RISK REDUCTION

Studies conducted in 2011 conclude that the use of psilocybin mushrooms is relatively safe, and that there are few reports of adverse effects, classified as “slight adverse effects”. The same studies indicate the importance of controlling both the quality and the context in which psilocybin mushrooms are used.

Physical Health

Due to the possibility of intense experiences that generate anxiety, people with a history of cardiovascular diseases, particularly those who are taking medication to control these diseases or who have to reduce their physical activity by medical indication, should refrain from using mushrooms.

Regarding the quality of the mushrooms, when collecting them in their natural environment it is essential to know how to identify mushrooms correctly and not to confuse them with any variety that may be toxic or poisonous. In general, only certain varieties of the genera Galerina and Pholiota have toxic or deadly effects and can be confused with psilocybin mushrooms.

Psychological health

Although mushrooms present few risks to physical health since psilocybin is pharmacologically a very safe substance, besides having no addictive potential, there are risks to psychological health that must be taken into account. Some of these risks may occur during the experience, and others later, in the medium term.

The main risk of psilocybin mushrooms is that they can trigger a difficult experience, in which there are unpleasant symptoms such as fear, anxiety, paranoid ideas, fear of death or going crazy, symptoms of a psychotic nature, or the feeling that the trip will never end. This type of experience can occur with any dose, although its manifestations in such cases are different.

At low and medium doses unpleasant psychological material can appear and the person may try to resist them; this resistance usually generates greater anxiety. In such cases, a change in setting can help reduce anxiety. A quiet environment and a willingness to surrender to the experience without judgment can often help to continue the journey and resolve these difficult moments.

At high doses, resistances are lower due to the intensity of the experience, and people are usually totally immersed in the trip. In such cases, difficult experiences may occur in which there is high emotional intensity, cathartic expressions, and unusual psychological manifestations of a “psychotic” nature, which usually disappear when the pharmacological effect diminishes. In these situations, physical and emotional restraint is needed, as is support

during the experience by a caregiver, preferably sober.

After difficult experiences there may be subsequent psychological challenges of a different nature that affect the person's health beyond the original experience. Symptoms of acute stress may appear after a traumatic experience with mushrooms that persist over time and require specialized psychological attention. Although the appearance of severe and persistent psychiatric disorders after the use of psilocybin mushrooms may occur, it is very rare. In cases of experiencing psychological difficulties after a psychedelic experience, psychotherapeutic integration sessions can help to alleviate the symptoms and process the psychological material of the session in an appropriate way.

Most difficult situations can be prevented by seriously considering the context in which the experience will be undertaken, the dose, the company and the vital moment in which one decides to use mushrooms.

Regarding the context, the usual recommendations regarding "set & setting" are especially important when using psilocybin mushrooms. A quiet, safe environment, free of interruptions and unexpected interferences, aesthetically pleasing, with music previously selected and especially with the company of trusted people is suitable for the type of experience that mushrooms induce. Less controlled and safe environments involve a greater possibility of unexpected events that can create anxiety. It is therefore essential to take into account what context the mushrooms are going to be used in and decide on the elements that will be a part of it.

It is also important to be psychologically prepared when taking mushrooms. A good theoretical knowledge of the potential effects that can appear at each dose can help with going into the experience with greater confidence.

Mushrooms, like any other psychedelic substance, have the potential to allow unconscious material to emerge. Therefore, it is crucial to take into account one's psychological state at the time of taking the mushrooms. Psilocybin mushrooms consumed during times of stress, worry, depression or life difficulties can increase the intensity of such symptoms.

Although from a therapeutic perspective it is considered that this is precisely the mechanism by which psychedelic substances can be useful in psychotherapy, it must be clearly known that the experiences induced by mushrooms can be intense and involve difficult emotions challenging to navigate if one is going through a complicated time.

A good foundation and emotional stability, as well as good preparation, a thoughtful context, in the company of trustworthy people, and a willingness to dive into the experience, whatever may happen, are factors that can contribute to a pleasant and fruitful experience with mushrooms.

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IPOMOEA VIOLACEA

IPOMOEA VIOLACEA

After the Spanish conquest of Mexico in 1521, several Spanish writers recounted the religious rituals of the Aztecs and other native groups that used the seeds of the *Rivea corymbosa*, called ololiuqui, for its intoxicating effects. Ergine, or LSA, is the main alkaloid responsible for these effects. Other botanical varieties contain the same psychoactive alkaloids, such as the lysergic rose (*Argyreia nervosa*) and rye ergot.

BASIC INFO

There are different plants around the world that contain alkaloids from the lysergic acid family. Some of the best known are the *Ipomoea violacea* (Morning Glory), the *Ipomoea tricolor* (*tlitliltzin*) and the *Rivea corymbosa* (*ololiuqui*). These alkaloids are also present in the fungus *Clavíceps purpurea*, known as ergot. All these plants have been used since ancient times for their psychoactive and medicinal properties.

Rivea or *Turbina corymbosa*, also known as piule by the Mazatecs, a-mu-kia (medicine for divination) by the Chinantec and ololiuqui and xixicamatic by the Aztecs, is a woody and large vine of the convolvulaceae family. It is a plant native to Central and South America. It has large leaves and white, bell-shaped flowers with brown seeds.

Ipomoea violacea and the *Ipomoea tricolor* are two varieties that are often confused and which some authors believe are the same. They are also perennial vines of the convolvulaceae family and native to North America and Central America, although their cultivation has spread throughout the world. They produce purple and blue flowers, respectively, and their seeds are black. The seeds of different varieties of Ipomoea have been used by the Zapotecs, who knew them by the name of bandungas or black badoh, to distinguish it from badoh, which was what they called the *ololiuqui*. Another name used was "the seeds of the virgin". *I. violacea* is commonly known in Mexico as the plate breaker, a term derived from the Mixe name.

Clavíceps puprúrea is a fungus, also known as ergot, which is a parasite on certain cereal crops, particularly rye. In this case it is known as "ergot rye" because of its dark horn shape that appears in the spikes. Its poisonous effects have been known Since antiquity and different episodes of poisoning occurred in the Middle Ages. Ergot poisoning was called "St. Anthony's Fire". Ergot contains psychoactive alkaloids, such as Ergine, but also toxic and poisonous ones, such as ergotamine and ergotoxin, which produce strong physical symptoms, such as gangrene and loss of limbs, which can obviously be fatal.

There are also other varieties that contain the same alkaloids as *Argyreia nervosa* (seeds of the Hawaiian rose), although it is unknown if they have been traditionally used.

A. nervosa is a climbing vine and one of the largest plants in the convolvulaceae family. Its leaves are large and heart-shaped, and it produces pink flowers similar to roses, so it is sometimes known as a "lysergic rose". It is native to the Indian subcontinent, although it is also found in Hawaii, Africa and the Caribbean. Its psychoactive effects have not been known until recently, although in Ayurvedic medicine it was used for therapeutic purposes.

ORIGIN / HISTORY

A report from the time of the Spanish conquest of Mexico states that the Aztecs had an herb that they called "cóatl-xoxouhqui", or green serpent, that contained seeds called ololiuqui. A Spanish missionary said of ololiuqui that it deprived those who consumed it of reason, and that it was the way that the natives communicated with the devil and experienced visions attributed to the deity contained in the seeds.

This plant was illustrated in the Florentine Codex by Friar Bernardino de Sahagún, who also described the medicinal

uses of seeds to treat gout and "aquatic fever", probably malaria, in combination with other psychoactive substances, such as mushrooms, peyote and the daturas.

The use of these seeds by the Aztec peoples is documented in both reports as well as murals, such as the one in Teotihuacán, dating from 500 CE, in which an Aztec mother goddess and her priests are represented under an ololiuqui vine. The piuleros of Oaxaca used them for divination and the Mayans used the seeds in an agave mead beverage to enter a trance as well as to treat tumors.

While not used for its psychoactive properties, *Argyreia nervosa* has a long tradition of use in Ayurvedic medicine. It has been used to treat such varied ailments as bronchitis, restlessness, tuberculosis, arthritis, diabetes as well as skin diseases and anorexia. It is also used as a medicinal plant in the Indian state of Assam, among the Lodhas and Santali people. All different parts of the plant have been used for these medical purposes - leaves, seeds, roots and fruits.

Relationship with the Eleusinian Mysteries

In Ancient Greece, secret rites in honor of the goddess Demeter were celebrated in the month of September annually for almost two thousand years. These initiatory rites occurred in the city of Eleusis, and during their celebration the myths of Demeter, the goddess of agriculture and fertility, and her daughter Persephone, who was kidnapped by the underworld god Hades, were recounted. During the time that Persephone remained stuck in the underworld, the earth froze as Demeter was busy looking for her daughter, and thus winter came to be. After her release, Persephone reunited with her mother, returned life to earth and spring appeared. The agreement reached by Hades and Demeter was that Persephone would spend one third of the year in the underworld, the winter period, and the rest of the year with her mother, thus giving rise to the three seasons of the year distinguished by the Greeks.

In the course of the Eleusinian mysteries, the initiates participated in a secret ritual in the telesterion, the main hall of the initiatory rite, in which a potion called kykeon was ingested. After its ingestion, the priests, called hierophants, performed stagings of the myths and the initiates experienced a vision, "they saw". After the initiation, the participants became "someone who had seen", an epopte. What happened in the telesterion and the visions of each epopte were secrets that were forbidden to be revealed under penalty of death.

Theories about the composition of kykeon suggest that it was an infusion containing rye ergot alkaloids, Ergine/LSA (lysergic acid amide), and that it was therefore a psychoactive potion. Unlike toxic alkaloids, Ergine/LSA is soluble in cold water, so it is hypothesized that an ergot infusion could extract just the psychoactive alkaloids and separate them from the toxic ones.

CHEMICAL COMPOSITION AND DOSAGE

The different varieties of *Ipomoeas* and *Argyreia nervosa* contain alkaloids of the lysergic acid amide family. The main alkaloids present and responsible for the psychoactive effects are the D-lysergic acid amide, known as Ergine and LSA/LA-111, and to a lesser extent isoergine, chanoclavine and elymoclavine.

Isoergine does not have psychoactive effects in doses of up to 2 mg, although it does have sedative effects, and may have psychoactive effects in higher doses.

The seeds of *A. nervosa* have the highest concentration of alkaloids of all botanical varieties. The approximate content is 3mg of alkaloids per gram of seeds. Of these alkaloids, 22.68% is Ergine (LSA), 31.36% is isoergine, followed by the LAE (lysergic acid ethylamide), iso-LAE, chanoclavine, elimoclavine and ergometrine in smaller percentages.

The seeds of *I. violaceae* are about 5 times less potent than the seeds of *A. nervosa*. According to Albert Hofmann's analysis, the seeds of the *Rivea corymbosa* (*ololiuqui*) contain 0.012% alkaloids, while those of the *Ipomoea violácea* contain 0.06%.

Dosage of Ergine

The doses of LSA/Ergine have not been clearly established, since there is no research in humans and there are hardly any reports regarding the use of the pure substance. Albert Hofmann, the discoverer of LSD, reported medium-strong effects with a dose of 500 micrograms administered intramuscularly, and later placed the active

dose between 1 and 2 mg orally.

Dosage of seeds

The seeds from plants containing LSA are usually ground and left to soak in cold water for several hours. The water is then filtered and swallowed. Some preparations are also made through alcoholic extractions, or by mixing the filtered water with alcoholic beverages.

There is no uniformity in the dosage of seeds used. Different varieties have distinct concentrations of alkaloids and each plant's potency is also influenced by its growing conditions. Therefore, many reports contain widely ranging information regarding the quantity of seeds used.

The Chinantecs and Zapotecs of Oaxaca often use thirteen powdered *ololiuqui* seeds (*Rivea corymbosa*).

Doses of *A. nervosa* are usually four to eight seeds. It is usually recommended to scrape the whitish layer that covers the seeds to reduce vomiting and gastrointestinal discomfort, although in many cases the seeds that are ultimately acquired do not have this layer.

Doses of *Ipomoeas* are somewhat more confusing due to the ambiguities in the taxonomic classification of the different varieties. The quantities of *I. violacea* seeds are between 5 and 10 grams, around 6 to 13 seeds. In the case of *I. tricolor*, 50 to 400 seeds are required.

EFFECTS

The effects of seeds containing Ergine/LSA are commonly compared with the effects of LSD. However, in different studies and user reports on the effects of *Ipomoea* and *Argyreia* seeds, no classical psychedelic effects are described, and the predominant effects are sedation and fatigue, with a small presence of perceptual and cognitive changes, such as an alteration in the perception of colors and mood elevation.

Therefore, the effects of seeds containing Ergine/LSA should not be compared to those of LSD or other classical psychedelics, because although they can provide experiences in which there is introspection and slight perceptual changes, their main effects are sedative and not psychedelic. In addition, Ergine has somatic effects that LSD lacks, such as unpleasant body sensations and feelings of intoxication.

The effects, when the seeds are ingested orally, usually occur between 40 and 90 minutes after ingestion, and the maximum effects are reached at 2 or 2 and a half hours. The total duration of the effects is usually about 5 - 8 hours, although in some cases the effects persist for longer.

Physical effects

The seeds of *Ipomoea* and *Argyreia* have quite noticeable and unpleasant physical effects, such as abdominal pain, nausea and vomiting, dizziness, fatigue and vertigo. There is also an increase in blood pressure and muscle tremors may appear. There is a certain drowsiness and decrease in motor activity for most people.

Psychological effects

The majority of reports from people who have consumed seeds of *Ipomoea* or *Argyreia* describe effects such as sedation, apathy and lethargy, and at higher doses visual phenomena can appear, in the form of geometric patterns, intensification of colors, and changes in perception and in self-image.

The sensation of drowsiness and of living in a dream state has been described, in which there can be a sensation of insight, thoughts of a philosophical nature and during which confusion can also present.

LEGAL STATUS

In most countries the pure substance is controlled and it is illegal to sell and possess. Ergine/LSA is a controlled substance in the United Kingdom on list A, as a precursor to LSD. In the United States it is included on Schedule III.

However, plant products that contain LSA, like the seeds of these different plants are not controlled, and therefore are legal to sell and own. The cultivation of these plants is not controlled.

IPOMOEA VIOLACEA

PREVALENCE OF USE

There are few studies that have quantified the prevalence of use of plants that contain LSA, although the available data indicate that it is very minor. The 2017 Global Drug Survey report indicates that 2.1% of respondents had used *Argyreia nervosa* at some time in their lives. In this survey, it was the second least consumed substance by respondents. When asked about the consumption during the last year, no plant that contained LSA appeared in the results of the survey.

According to data from 2005 of the National Institute of Toxicology and Forensic Sciences of Spain, only 1% of the calls responded to are due to poisoning with plants (422 in total), and of them only 1.2% were related to *Argyreia nervosa* (5 calls).

The report of the Spanish Observatory of Drugs and Addictions does not collect any information about plants that contain LSA.

HEALTH AND RISK REDUCTION

One of the most notable difficulties when using seeds that contain LSA is the variability of potency of the different varieties, and even the variation of potency in seeds of the same species. In addition, it can be difficult to identify the actual variety of seeds that are being used. Therefore, it is difficult to control the dosage.

Analysis of products sold as *legal highs* with the same trade name have observed that these may contain a variable amount of alkaloids, so their potency may also vary depending on the batch and the seeds from which the product comes.

Added to this difficulty is the variability in individual responses. In studies with standardized doses different people have had profoundly variable effects at the same dose, suggesting that each person may have a very different response to this substance.

Medium and high doses have caused episodes of confusion, mental disorganization and even temporary psychotic symptoms in at least two cases documented in the scientific literature, as well as very unpleasant physical effects. Therefore, although most reports claim sedative effects and low psychoactivity, it is important to be cautious with the amount of seeds used.

In combination with other substances such as THC/cannabis and alcohol more intense effects have been reported, and there has been one case of suicide under the effects of these combined substances.

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AYAHUASCA

AYAHUASCA

The word “ayahuasca” is a Quechua term composed of two words: aya, which means “corpse, dead, dead human body.” and waskha, which means “rope, cord, braided or twisted wire.” Thus, it has commonly been translated as “the vine of the dead” or “the rope of the dead.”

BASIC INFO

Ayahuasca is a decoction of the Amazonian vine *Banisteriopsis caapi.* Its chemical ingredients are known as harmalines. Some ethnic and religious groups add the *Psychotria viridis* plant to ayahuasca, which has visionary effects and whose active component is dimethyltryptamine (DMT).

The word ayahuasca refers to both the preparation made with *Banisteriopsis caapi* to brews wherein which other Amazonian medicine plants are added, which today is most common.

Other names that diverse communities and groups use for the preparation are: Caapi, Dápa, Mihi, Kahí, Natem, Pindé, Yajé, Daime, Vegetal, among many others.

Many different recipes exist for the preparation of ayahuasca, and some preparations contain only the *B. caapi* vine, although this is not common. Ingredients added to the decoction depend on the region in which it is prepared, the curandero or vegetalista that cooks it, and the intention or effects that are desired. Over 100 different botanical species that have been used as additives to ayahuasca have been documented.

The most popular additive in the West is *Psychotria viridis*, which results in the combination most commonly understood as ayahuasca – that of *B. caapi* and *P. viridis*. *Diplopterys cabrerana* is another common plant that is used instead of *P. viridis*, depending on availability in the region.

B. caapi contains beta-carbolines (harmine, harmaline and tetrahydroharmine) and *P. viridis* and *D. cabrerana* are sources of dimethyltryptamine (DMT). The combination of these alkaloids allows DMT to have an oral effect because in the absence of beta-carbolines the DMT would be degraded by monoamine oxidase (MAO) present in the human body.

Banisteriopsis caapi is a vine of the Malpighiaceae family that grows throughout the amazonian forest. Its structure is that of woody, braided vines that climb different trees, with large leaves that can reach 18 cm long and 8 cm wide. The plant is referred to as ayahuasca, caapi, or mariri, among other names.

Popularly known as chacruna, *Psychotria viridis* is a perennial shrub from the Rubiaceae family, the same family as coffee, which produces fruit similar to coffee beans. It grows in the jungles and rainforests of Central and South America, although it is most commonly found in the Amazonian areas of Peru and northern Bolivia. It can reach up to 5m in height.

ORIGIN / HISTORY

The origin of the use of ayahuasca, as well as the origin of its use, are unknown. Different authors have proposed varying theories about the origins of ayahuasca, and since the expansion of ayahuasca, popular culture has tended to emphasize the ancient origins of the use of the decoction by native Amazonian peoples.

Some authors have proposed that the use of ayahuasca dates back 5000 years, others date its first use to between 500 BC and 500 AD. Other theories point to much more recent origins.

Unlike other New World drugs, such as psilocybin mushrooms, datura, peyote, psychoactive rapés or ololiuqui seeds, there are no archaeological remains that demonstrate the existence of the ancestral use of ayahuasca. The use of the former can be proven, given that there are drawings in codices with representations,

reports from missionaries of their use, sculptures and, in the case of rapé, remains of instruments for its use. However, this is not the case for ayahuasca.

The first accounts in which the word ayahuasca appears are those of Jesuit missionaries who, in 1737 and 1740 respectively, travelled through the Napo River area. The use of ayahuasca for curative and divinatory purposes is mentioned in their reports. There is an earlier account from another Jesuit at the end of the seventeenth century, in which he mentions a "diabolical brew," while not explicitly mentioning ayahuasca.

The first modern and scientific report of the use of ayahuasca was in 1851, in which Richard Spruce documented the use of the medicinal concoction in Brazil. Then, in 1857 Manuel Villavicencio wrote the first known account of a subjective experience with ayahuasca.

It is significant and surprising that there are no references reference to the use of any type of potion or brew (as indeed there are to other substances) in earlier accounts of colonizers and missionaries who exhaustively traveled the Amazon basin as well as the Napo River, which seems to be the most plausible place for the first use of ayahuasca.

Brabec de Mori has proposed a centuries-long history of the use of ayahuasca, based on an analysis of the icaros, the songs used during ayahuasca ceremonies. According to this author, the Tucano people of the Napo River basin began to use ayahuasca in relatively recent times, and both its use and the songs expanded from there. Brabec de Mori analyzed similarities between the icaros of different tribes, and compared them with other traditional songs of these peoples. While the traditional songs were very different among the groups, their icaros were very similar, which led to him to conclude that they have a recent common origin.

B. caapi grows in the Amazon lowland forest, from the south of Bolivia to the north of Panama, in the Amazon of Peru, Ecuador, Colombia and Brazil. It seems reasonable to assume that the use of *B. caapi* predated the use of it in combination with *P. viridis*, and that it was used as a purgative. It also seems reasonable that different indigenous groups added different plants to this decoction, and that it was through these experiments that the powerful effects of the combination with chacruna were discovered.

Indigenous peoples who used ayahuasca traditionally or who use it today include: Guahibo, Shipibo-Conibo, Shuar, Colorado, Ingano, Siona, Kofan, Witoto, Tukano, Desana, Yakuna, Ashaninka, Kaxinawa, and many others .

The Ayahuasca Churches

Another context for ayahuasca use that has arisen in the last century encompasses the ayahuasca churches, such as the Santo Daime (with its multiple branches), the União do Vegetal (UDV), and Barquinha. These churches are syncretic religious sects that combine shamanic, esoteric, spiritualist and Christian elements, among others, around the ritual use of ayahuasca, daime or hoasca, as the drink is called in these settings.

These churches appeared at the beginning of the 20th century, founded by Raimundo Irineu Serra (later known as Mestre Irineu), a rubber tapper who, after spending time in the jungles of the state of Acre of Brazil, began to officiate ceremonies with ayahuasca. Irineu spent time with healers who taught him how to collect the necessary plants and to prepare ayahuasca. He spent time alone in the jungle experimenting with the decoction, and in his visions he received "hymns," ritual songs transmitting teachings and that are sung during the "trabalhos" (Portuguese for "works") as the Santo Daime members refer to their ayahuasca ceremonies.

This doctrine grew more sophisticated and became the Santo Daime, which the evolved into different branches, growing in terms of numbers of followers and expanding internationally. One of the most widespread branches, and what is commonly known as the Santo Daime, is the ICEFLU (Igreja do Culto Ecléctico da Fluente Luz Universal or Church of the Eclectic Cult of the Fluent Universal Light), formerly CEFLURIS. This group was founded by Sebastião Mota de Melo (known as padrinho Sebastião).

The União Do Vegetal is a church with origins that are more urban than the Santo Daime, founded by José

Gabriel da Costa (known as Mestre Gabriel), which also arose in the state of Acre.

The third main church is the Barquinha, although it has not expanded internationally and exists only in Rio Branco, in the state of Acre, Brazil. The Barquinha was founded by Mestre Daniel.

Some estimates suggest that the number of people belonging to these religions is more than 25,000 worldwide. The Santo Daime and the UDV have expanded internationally and groups can be found in countries as diverse as Brazil, the United States, Canada, Spain, Holland, Germany, and even Japan. In some of these countries, churches have legal protection of their religious practices, including the use and importation of ayahuasca.

CHEMICAL COMPOSITION AND DOSAGE

As indicated above, ayahuasca is a preparation of different plants, although the usual combination is made with the *Banisteriopsis caapi* vine and the leaves of *Psychotria viridis*. The vine is usually crushed or pulverized and cooked together with the leaves in a process that can be very elaborate, until the desired amount and concentration is obtained.

The alkaloids present in ayahuasca potions are a combination of beta-carbolines and tryptamine derivatives.

Beta-carbolines

B. caapi contains the beta-carboline alkaloids harmine, harmaline and tetrahydroharmine (THH). These alkaloids perform a specific effect as reversible inhibitors of monoamine oxidase-A (MAO-A), which allows DMT to be active orally.

The oral dose of harmine that causes perceptible effects is around 8 mg/kg.

Analysis of ayahuasca brews have found harmine at quantities of about 158mg per dose, which would be equivalent to a dose of about 2mg/kg for a person weighing around 70kg. This amount is sufficient to cause the inhibitory effects of monoamine oxidase, which allows the DMT to be orally effective.

In their bioassays, Jonathan Ott and other authors found that the minimum amount of harmine needed to induce the oral activity of DMT was about 70mg to 150mg, or around 1mg/kg to 2mg/kg.

Tryptamines

The leaves of *P. viridis* (or *D. cabrerana*) contain the alkaloid derived from the tryptamine N, N-dimethyltryptamine. DMT is a potent substance with visionary effects when administered intravenously or vaporized, but that is orally inactive because it is degraded by the MAO present in the stomach and liver. There are more than 50 known plants that contain DMT in varying amounts and it is possible that it is also found in the nervous system of mammals, including the human brain.

DMT dosage oral administration (in combination with harmalines)

The dose range of DMT in the presence of harmalines or other MAO inhibitors varies from 0.5mg/kg to 1mg/kg. So, for a person weighing 70kg the doses would be the following:

» Threshold dose: 30mg
» Average dose: 50mg
» High dose: 70mg

Ayahuasca dosage

Ayahuasca is usually dosed or administered in varying amounts, depending on the potency or concentration of the decoction, which is usually known by the healer/curandero or group who brewed it. The concentrations of alkaloids in ayahuasca vary widely. Callaway conducted an analysis of ayahuasca from the UDV, Santo Daime, Barquinha, and Shuar peoples, and the alkaloid ranges present were as follows:

» DMT concentration: between 0.16mg/mL and 14.15mg/mL (although some samples did not contain any DMT)
» THH concentration: between 0.49mg/mL and 23.80mg/mL
» Harmaline concentration: between 0.01mg/mL and 0.9mg/mL
» Harmine concentration: between 0.45mg/mL and 22.85mg/mL

Customary dosages depend on the tradition. In the Santo Daime doses tend to be between 50 and 100 ml, among the Shuar from 20 to 30 ml, in the UDV from 100 to 200 ml.

In ayahuasca ceremonies, two or three doses are usually consumed, distributed over the multi-hour session.

Other added substances

In many instances, other plants are added to the ayahuasca brew, depending on the region, indications and intentions. Traditionally, ayahuasca cooked by the Santo Daime, UDV and Barquinha (known as Daime, Vegetal or hoasca) contains only *B. caapi* and *P. viridis*, while it is more common to find other plants in addition to these two in the preparations of the indigenous peoples of Peru, Ecuador and Colombia.

The following are some of the plants that are usually added to ayahuasca and their main alkaloids:

Nicotiana rustica: The tobacco plant, with purgative and psychoactive effects. Contains nicotine.

Brugmansia suaveolens: Known as toé or floripondio. Contains tropane alkaloids, such as scopolamine and hyoscyamine, that have hallucinogenic effects with dangerous toxicity.

Brunfelsia grandiflora: Known as chiric sanango. Used as a medicinal plant in the Peruvian vegetalista tradition, and as a plant used for "dietas."

EFFECTS

Ayahuasca is a powerful visionary substance due to its alkaloids – DMT and beta-carbolines. Although it appears that the most prominent effects are due to DMT and not to beta-carbolines, since studies carried out with beta-carbolines have been inconclusive, the effects of each alkaloids will be described separately below.

DMT is a 5-HT2A serotonergic receptor agonist and its effects are described as being similarly to those of the so-called "classical psychedelics" (LSD, psilocybin, mescaline). DMT, when not administered in combination with MAOIs and taken intravenously or smoked, produces intense and immediate effects, including:

» An immersive experience
» Intense visual phenomena with both open and closed eyes
» Kaleidoscopic visions
» Changes in time perception
» Alteration of auditory perception
» Profound and spiritual, as well as terrifying, experiences
» Experience of contact with entities

The psychoactive effects of THH, harmine and harmaline are not well defined. Although the importance of them in ayahuasca preparations as monoamine oxidase inhibitors is clear, their contribution to the subjective effects is not well understood. Different studies have reported disparate effects of harmaline. Authors such as Claudio Naranjo and Alexander Shulgin have reported psychoactivity and hallucinogenic effects, while Jonathan Ott reported simply sedative effects like those experienced with diazepam, and other authors have not found any psychoactive effects at all.

Interestingly, within the shamanic worldview the plant is credited with endowing wisdom to the decoction and that which allows learning is *Banisteriopsis caapi,* ayahuasca, being the plant that contains beta-carbolines, while it is believed the leaves of the *Psychotria viridis* simply provide visions and color. This indicates an entirely different conception of the desired effects depending on the culture of those who use ayahuasca.

AYAHUASCA

The general effects of ayahuasca can be understood as a combination of the effects of the different alkaloids it contains rather than as a mere oral activation of DMT.

The effects produced by ayahuasca can include:

» Perceptual and cognitive changes
» Distortion of temporal perception
» Visions with eyes open and closed
» Increase in associative thinking
» Introspection
» Increase in autobiographical memories
» Mood elevation
» Profound and spiritual experiences
» Experiences of anxiety, fear and even terror
» Experiences of contact with entities or spirits

On the physical level, the following effects may be experienced:

» Dizziness
» Physical discomfort
» Nausea and vomiting
» Diarrhoea
» Seizures (rarely)

The anxiolytic, antidepressant and anti-addictive effects of ayahuasca and other 5-HT2A agonists such as LSD and psilocybin have been reported in controlled settings.

PREVALENCE OF USE

Although the use of ayahuasca has expanded globally in recent years, and the number of people who use it is rising, ayahuasca continues to be a substance that is not widely used.

According to the Global Drug Survey carried out in 2015 and 2016, only 527 people out of the 96,901 who participated claimed to have used ayahuasca at some time in their lives. This represents 0.57% of the sample. It could be argued that the sample has a considerable bias given that it is based on people who have self-selected, and who have encountered the survey through their online communication networks. It could be argued that people who use ayahuasca may use different communication channels and therefore may have not been aware of nor answered the survey.

The subjective observations by ayahuasca community participants is that the number of retreats and events where the use of ayahuasca is offered has increased greatly in the last five years in Europe, the United States, Latin American countries, and especially in Peru, where centers offering retreats with ayahuasca have multiplied and ayahuasca tourism has increased to become an important part of the economy, especially in the Iquitos region.

LEGAL STATUS

The psychoactive alkaloid present in ayahuasca, DMT, is a Schedule I controlled substance according to the 1971 United Nations Convention on Psychotropic Substances. As such, DMT is considered a substance whose use, manufacture and sale are prohibited – except for very limited medical and scientific uses. However, the ayahuasca decoction itself is not under international control, which has been confirmed by the International Narcotics Control Board (INCB). In practice this has been interpreted in different ways by governing bodies and at the national level ayahuasca has been subject to three different legal approaches.

The first approach has been applied by countries where certain contexts for ayahuasca ayahuasca are permitted, and sometimes regulated – such as religious use for churches in Brazil, the United States and Canada – or traditional use in Peru, where it is considered a national cultural heritage (Peru made areservation for these traditional uses of ayahuasca when signing the the 1971 Convention). Countries that exhibit the second approach – wherein ayahuasca is specifically prohibited – include France (whose regulatory lists include various plants used in the decoction) and Russia, where ayahuasca is considered illegal because all plants containing

psychoactive ingredients are prohibited.

The third legal approach encompasses countries where there is a legal void with regards to ayahuasca – it is not specifically prohibited, but it is not permitted, and several people have been prosecuted for receiving the brew by mail or bringing it with them on a plane. This is the case in countries such as Portugal, Mexico, Israel and Spain, the country which has the highest number of legal incidents related to ayahuasca recorded in recent years. It is important to be well informed about the legal status of ayahuasca in each country to prevent possible legal incidents – the Ayahuasca Defense Fund's legal map is a good tool for this.

HEALTH AND RISK REDUCTION

Studies in both animals and healthy humans have shown that ayahuasca is a safe substance both physically and psychologically when its composition is known, and when it is administered in controlled doses, in appropriate environments and with the necessary support.

There are some risks associated with the consumption of ayahuasca that should be considered in case one is considering using this decoction. Some of these risks are physical, due to the pharmacology of the substance and possible interactions, and others are psychological, due to the nature of the experience that ayahuasca can induce.

Physical Health

Some of the physical risks of ayahuasca are related to the presence of beta-carboline which have an inhibitory effect on MAO-A. In theory, the combination of MAO-A inhibitors with certain foods containing high amounts of tyramine could produce a hypertensive crisis, and the combination of MAO-As with other chemical substances (medications, drugs) can involve significant risks. The combination of MAOIs with SSRIs (selective serotonin reuptake inhibitors), other antidepressants, or tryptophan beforehand could produce a serotonergic crisis called serotonin syndrome. While this risk is posited theoretically – there are no documented cases of such interactions – most guidelines regarding the consumption of ayahuasca highly recommend avoiding this combination.

For the same reason, combining of ayahuasca with ginseng, hypericum or with drugs and medications such as dextromethorphan, amphetamines and MDMA, can be potentially dangerous and should be avoided.

Some providers of ayahuasca sessions are offering retreats in which ayahuasca and Bufo alvarius are also used. Ayahuasca is usually ingested a few hours before or after smoking this toad poison, which contains bufotenin and 5-MeO-DMT. This combination carries certain risks that must be considered in order to avoid adverse reactions, and it is recommended to wait 24 hours between the use of each substance. For more information:

http://news.iceers.org/es/2017/05/alerta-bufo-alvarius-con-ayahuasca/

Psychological health

The psychedelic effects of ayahuasca can be very intense and the experience can be quite immersive, therefore it is not uncommon for reactions of fear and anguish to occur during parts of the experience. These situations are usually transient and resolve themselves during the experience or after the effects of the substance subside.

However, some people do experience adverse effects following the experience, particularly if it was especially difficult, if the setting in which they took ayahuasca was not safe, or if they did not receive adequate support during and after the experience.

The occurrence of a difficult psychological reaction is the main risk associated with the use of ayahuasca. Reactions can include panic attacks, fear of dying or going crazy, terrifying encounters with entities/spirits, and in some cases symptoms of psychosis.

Studies of long-term ayahuasca use found that people who have used ayahuasca for at least 15 years scored

lower on psychopathology scales than the control group, and higher on life purpose and markers of wellbeing. However, we must bear in mind that there is a bias in the selection of people who participated in these study as the people for whom ayahuasca did cause problems did not continue consuming it and were therefore not included in the study.

Other studies have investigated the occurrence of serious adverse effects, such as psychotic reactions that last more than 48 hours, which are serious episodes even if they occur with very low frequency. These episodes have not occurred in controlled research settings where participants have passed a physical and psychological screening. People with a family history of psychotic episodes, or with diagnosed mental disorders such as schizophrenia, bipolar disorder, and depression with psychotic symptoms are at higher risk of suffering such adverse reactions and it is recommended that they refrain from using ayahuasca.

Important elements to take into account to reduce risks and maximize the potential benefits are: choosing the appropriate place and setting within which to take ayahuasca, as well as the person that will lead the session. Ayahuasca is usually used within ritualized contexts and the person facilitating the session can have a powerful influence on how the experience unfolds, the dynamics generated by the group, safety, as well as the maintenance of ethical and responsible boundaries with participants. The number of reports of malpractice by facilitators of ceremonies is growing, due to lack of knowledge, experience, and training, as well as a lack of ethical and respectful interactions with participants. It is therefore recommended to inform oneself extensively about the group or place with whom one intends to take ayahuasca, the format of the ceremonies, the number of participants and assistants, as well as asking about the training, experience and references of the person who will guide the ritual.

For an overview of the most important aspects to maximize the safety of the ceremonies in which ayahuasca is used, consult the ICEERS Good Practice Guide:

http://iceers.org/Documents_ICEERS_site/Safety&Ethics/Ayahuasca-Good_Practice_Guide_ICEERS2014.pdf

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AYAHUASCA

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IBOGA

IBOGA

Tabernanthe iboga is a shrub native to Central West Africa traditionally used in rites of passage and healing ceremonies. Its main alkaloid is ibogaine, which has been used since the 1960s for the treatment of addictions.

BASIC INFO

Ibogaine is the most researched of the known iboga alkaloids. It is estimated that the plant's other alkaloids could also have therapeutic properties. Iboga has been shown to be effective in reducing addiction severity, eliminating the withdrawal syndrome associated with opioid use, and in reducing the compulsive desire to consume a wide variety of drugs. The iboga experience can facilitate a deep review of one's personal history and current situation as well as modification of behavior and perceived role in family and society.

ORIGIN / HISTORY

The root bark of the iboga plant has played a fundamental role in rites of passage and healing ceremonies of many tropical African cultures. The plant is used in Cameroon, Equatorial Guinea, Congo, Zaire and especially in Gabon by the pygmy people, as well as the Fang and Mitsogo Bwiti cultures. Etymologically, "Bwiti" is roughly translated as "ancestor" or "dead", but may originate from the word "Mbouiti", the accurate name for the pygmy people located between Gabon and Zaire.

Traditionally, iboga is used in Bwiti adolescent rites of passage or in healing ceremonies for both men and women, separately. The ritual surrounding iboga lasts five days and at the individual undergoes a process of death and rebirth, carefully guided by the community through the performance of a series of rituals in which many people take part; a symbolic death of the adolescent or of evil gives way to the birth of the adult or healthy person.

Ibogaine in modern society

In 1962, Howard Lotsof, a young man from New York with a heroin dependency, along with six other heroin-dependent friends, conducted an experiment. They ingested ibogaine and the next day, six of the seven friends stopped using heroin, since they had no withdrawal syndrome or desire to consume. In the following years, efforts to ensure that ibogaine would be considered a valid alternative for the treatment of opiate addiction obtained little response from the pharmaceutical industry. NIDA (National Institute of Drug Abuse) developed a 4000-page Drug Master File (DMF), including 16 volumes of pre-clinical studies. In 1993, the FDA approved a Phase 1 clinical trial, which concluded after the first treatment due to patent disputes. In 1995, NIDA decided not to continue supporting ibogaine research, but drug user groups and advocacy organizations promoted its use and made it available to the public in alternative non-clinical settings. The number of treatment providers and demand on behalf of those seeking to end drug dependency has grown exponentially in the last 10 years. There are ibogaine clinics in countries such as Brazil, Mexico, Thailand and South Africa, and treatment providers all around the world. In 2009, New Zealand was the first country in the world to accept ibogaine as a medication.

CHEMICAL COMPOSITION AND DOSAGE

The root bark of *Tabernanthe iboga* contains the alkaloids ibogaine, ibogaline and ibogamine in approximate proportions of 80%, 15% and 5%, respectively.

IBOGA

In the past, extracts from the bark of the plant have been used for different purposes, including the treatment of asthenia (in doses of 10–30mg daily), as a neuromuscular stimulant (in doses of 200mg of extract, about 8mg of ibogaine) and for the treatment of depression, fatigue and recovery from contagious diseases. These uses have not been properly investigated and there are currently no prescription medications containing ibogaine.

For the treatment of addictions, elimination of withdrawal syndrome and avoiding cravings, Lotsof recommended a dose of 15–20mg/kg of ibogaine. Doses above 12mg/kg are considered to carry a much higher cardiovascular risk because they can produce unforeseen physiological reactions, including fatality, so it is always recommended to consume these doses in controlled environments with health professionals trained in cardiac emergencies.

Another method that has been used to mitigate the withdrawal syndrome of methadone and other opioids to gradually reduce its use is the repeated dosing of small, increasing amounts of ibogaine. In one case, a total of 5 dosages were used, in amounts of 150, 300, 400, 500 and 600 mg of ibogaine. This dosing only produced mild psychological effects while allowing complete detoxification from methadone.

In personal growth and self-exploration contexts, high doses of bogaine, iboga or its extracts are commonly used, which produce an intense subjective experience. In these cases the doses are often similar to those proposed by Lotsof.

EFFECTS

Ibogaine induces an introspective experience that is often referred to as deeply psychotherapeutic. It is referred to as an "oneirophrenic" as it can induce a waking dream state, although this is not always the case. An experience with ibogaine is not considered hallucinogenic because the individual is usually aware of where he or she is, that the experience is caused by the ingestion of ibogaine and that the visions that one has during the experience are internal projections, although there are exceptions to this.

The initial phase of the experience can often consist of intense visual introspection lasting between 7 and 12 hours and is often saturated with information that may be experienced more objectively, as an observer, while deeper psychological integration of the content is not accessible. During the following 24 hours of the experience, the visionary phase ends and the contents of the experience can be integrated in a cognitive process. Subsequently, this integration process may continue to develop in daily life for months as the individual re-defines their identity and interpersonal dynamics related to their environment.

Anti-addictive effects

Despite the existence of a vast quantity of animal studies, only limited evidence is available on the effectiveness of ibogaine in humans, although an increasing number of studies, case studies and testimonies of substance-dependent people who have undergone this treatment support the findings regarding its potential as a tool for the treatment of addiction. Iboga seems to be especially useful for opioid addiction, and to a lesser extent (and with greater risks) in the treatment of addiction to cocaine and amphetamines. Ibogaine does not attenuate alcohol or benzodiazepine withdrawal syndrome, although it attenuated alcohol intake in animal studies and has been shown to be helpful anecdotally in humans.

Iboga has potent neuro-regenerative effects due to its complex interactions with different neurotransmitter systems. Ibogaine up-regulates the dopaminergic system and increases the production of GDNF (a protein that promotes the survival of certain neurons), which creates a unique state of neuroplasticity.

This combination of effects reduces the desire to consume certain substances and promotes the tendency toward new behaviors, which makes it an effective tool for both substance and behavioral addictions when used with the appropriate expectations and perspective.

Although some people are able to resolve their addiction with a single iboga administration, for many others this is unrealistic, as habituations can be deeply embedded and withdrawal symptoms and the desire to consume may

persist, often due to chronic nutritional deficiencies that may cause neuro-chemical imbalances.

Ibogaine can be a substance dependency interrupter and a catalyst for change and may provoke deep psychological insights and increased self-awareness.

LEGAL STATUS

Since the discovery of the anti-addictive properties of ibogaine in 1963, the global acceptance of its therapeutic application and its development as a medicine has been very slow.

Ibogaine is not on the international lists of controlled psychotropic substances of the United Nations International Narcotics Control Board, but it is illegal in the USA, Australia, Belgium, France, Switzerland, Sweden, Poland, Denmark, Hungary and Israel. In 2017, Health Canada added ibogaine to the Prescription Drug List noting that it was "not authorized for use in Canada."

PREVALENCE OF USE

Iboga is a relatively minimally used substance among circles of psychoactive plant users. It is not a substance that is commonly offered on the black market and only some exchange exists within opiate user circles. It is usually administered in centers or clinics that specialize in detoxification treatment. The range of these centers is extremely varied, from legal clinics that openly advertise their services and have medical equipment and personnel, to individual providers that administer ibogaine in apartments or rural homes to those seeking detoxification treatment.

Certain circles exist that use ibogaine with introspective, shamanic or spiritual intentions, doing retreats that provide an experience in settings oriented toward personal growth.

Sometimes rituals based on Bwiti tradition are performed, although these types of settings are not common. Certain Western ibogaine providers do incorporate elements of a variety of African traditions into their treatments, such as music, plant baths and ritual offerings.

In the 2018 survey conducted as part of the scope of this European Union funded project, out of 593 respondents, all users of some variety of psychoactive plants, only 60 answered yes to having ever used iboga. This percentage is one of the lowest, along with Khat, *Argyreia nervosa*, *Bufo alvarius* and the Datura.

HEALTH AND REDUCTION RISK

The greatest concern about the known risks of using ibogaine is that it decreases the heart rate (bradycardia) and prolongs QT intervals, a measurement of the time between the onset of the Q wave and the end of the T wave in the electrical cycle of the heart. Therefore, people with a history of myocardial infarction, murmurs, arrhythmias, heart surgeries or severe obesity should not take ibogaine. An electrocardiogram (ECG) is the absolute minimum test required, but a stress test and/or 24-hour monitoring with a Holter increases the possibility of detecting important abnormalities. The presence of a skilled physician (preferably a specialist in cardiology and emergency medicine) during the session, who monitors variations in heart rhythm and other vital signs, significantly increases the safety of this treatment.

Another risk factor is pulmonary embolism. This occurs when there are blood thrombi in the veins, such as those that can occur during prolonged immobility during airplane travel, car accidents or blood-related diseases. When these clots circulate through the body during an ibogaine session, they can reach the lungs, where they can cause an embolism with the risk of suffocation. The risk of pulmonary embolism can be reduced by doing sports or exercise after long, sedentary trips and by avoiding initiation of treatment immediately after arrival at the destined treatment location. People with bleeding problems, chronic blood clots, or people who have recently been involved in accidents that have caused bruising and bleeding should be excluded from treatment.

Medical conditions such as asthma, cancer, cerebellar dysfunction (e.g. Meniere's disease and difficulty in maintaining balance), chronic fainting, diabetes, emphysema, epilepsy, diseases of the intestinal tract (Crohn's disease, inflammatory bowel disease), gynecological problems, HIV, AIDS, Hepatitis C (if active with liver enzymes 200% above normal), kidney problems, liver problems, thyroid problems, tremors, tuberculosis and ulcers are also contraindications in most cases, but some centers accept people with certain ailments, increasing the treatment risk.

Another cause of adverse effects is the interaction of ibogaine with other drugs or pharmaceuticals. Before taking ibogaine, the recipient should avoid consuming drugs for a sufficient period of time to ensure that the drug has been eliminated. This depends on the half-life of the drug, and is different for each substance. On the other hand, foods and substances that are metabolized by the enzymes CYP2D6 (an enzyme involved in the metabolism of many drugs) should be avoided, since they could interact with ibogaine, and potentiate its effects of bradycardia and QT prolongation. There are lists of such substances available on the Internet. Quinine and grapefruit belong to this group and should be avoided before and during treatment.

Given that iboga is offered in such a variety of forms, taking a material whose chemical composition and potency are unknown is another risk factor. It is important to know the exact dose and composition of ibogaine to avoid overdose or complications.

Psychological Risks

Although some centers accept people with psychiatric disorders such as bipolar, borderline personality disorder, etc. – and certain patients do report an improvement in their condition – nothing is known about the effects of ibogaine on such disorders or the risks that it involves. It is a dangerous landscape. In general, people with psychiatric disorders such as those mentioned above, as well as those suffering from schizophrenia and a history of psychosis, must be excluded from this treatment, since ibogaine could cause the reappearance or worsening of symptoms. Similarly, the interaction of ibogaine with certain psychotropic drugs can be dangerous. An in-depth psychiatric review as well as the supervision of a psychiatrist is important before engaging in ibogaine treatment in case of the existence of a psychiatric disorder or the use of certain medications.

In addition to psychiatric risks, ibogaine is a powerful psychoactive substance that can induce an introspective experience that is not always easy to manage. Episodes of extreme anxiety can occur, and in more serious cases, paranoia. A skilled facilitator should be able to offer necessary support to the individual and assist with difficult episodes. Proper preparation with the guidance of a therapist can help greatly in improving self-confidence, going into the experience with an appropriate mental state and being prepared for possible difficult experiences.

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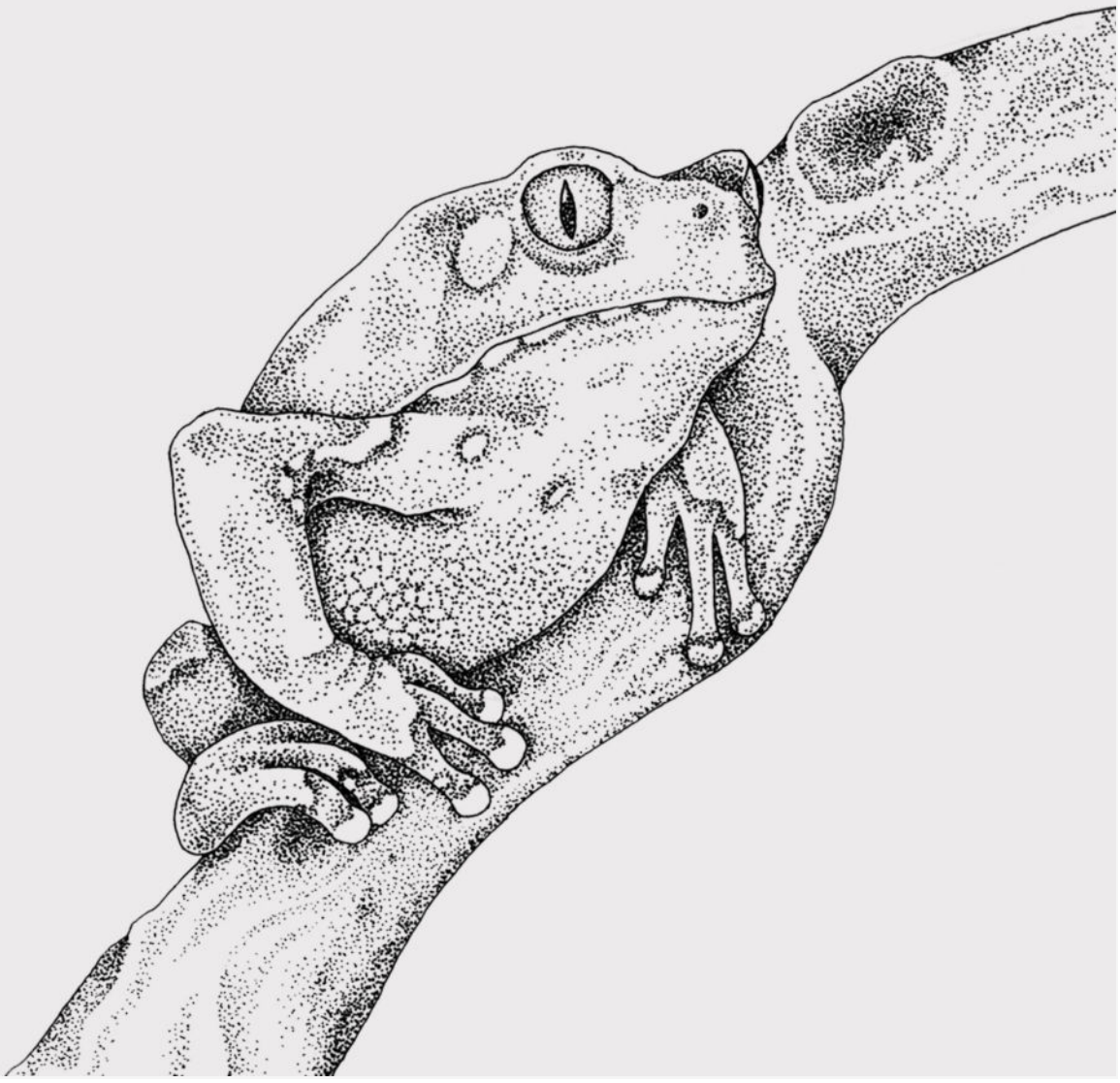
KAMBÓ



KAMBÓ

Kambó is the common name in South America to refer the skin secretions from *Phyllomedusa bicolor,* a tree frog that inhabits certain areas of the Amazon rainforest. It is also commonly known as "sapo" (the Spanish word for toad). It has been traditionally used as a medicine by indigenous tribes, such as the Katukina, Yawanahua, Cashinahua, and Matses.

BASIC INFO

Kambó has been traditionally used to provoke a deep cleansing of the body and the soul, to cure from "panama" (which could be translated as "bad luck in hunting"), to give strength, and to cure other diseases.

Kambó contains a high number of different bioactive peptides responsible for the physiological effects. The most characteristic being the stimulation of gastrointestinal motility, contributing to vomiting and diarrhea. It also causes a fall in blood pressure and tachycardia. Kambó presents no hallucinatory or psychoactive effects whatsoever. After application, acute effects appear within few minutes and may last for a range of five to twenty minutes depending on the applied dosage.

It is applied in a previously inflicted small and superficial wound created with a burned stick, traditionally known as titica vine (*Heteropsis flexuosa*). Then, the secretion previously hydrated is placed over the wound appearing like a "dot" the size of a green pea. It is generally applied on the arms or chest in men, or legs in women. The dosage and effect will depend on the number of dots applied.

ORIGIN / HISTORY

Traditional use of Kambó is geographically centered in the amazon rainforest, were the frog is found. This practice has been historically rooted in different tribes in regions of the Peruvian, Colombian and Brazilian amazon. Each tribe has its own story or myth about how they started the practice of Kambó, usually implying revelations in dreams or in altered states induced by plants.

To begin, the frog is captured and carefully tied up in an X shape. The frog will expel a skin secretion as a defense mechanism from predators. This secretion, stimulated by the stress of manipulating the animal, is collected in a bamboo stick and left to dry for storage. For traditional cultures, this is a medicine that operates on the physiology of the organism or the body, and also in the realm that is beyond material, i.e. the soul. Kambó is regarded as an entity or a spirit that is going to be the responsible for the healing process. In this scenario, the frog is treated with respect and never harmed for, according to Amazonian beliefs, harming it would anger the animal spirit and thus fail to heal. After the extraction, the frog is released back into the forest.

The missionary French priest Constantin Tastevin was the first, in 1925, to come along and register this practice in the upper Juruá river in Brazil. In the 1990's Kambó practices were learned by rubber tappers and they started to apply it in themselves and bring it to towns and cities in Brazil.

The knowledge of this practice has been gradually expanding in the western world. Nowadays is common to find offers of Kambó application in plant medicine retreats and find practitioners or even the substance itself advertised online

CHEMICAL COMPOSITION AND DOSAGE

The *Phyllomedusa bicolor* skin secretion contains a very high number of bioactive peptides (short chains of aminoacids that can bind to cell receptors in human cells and trigger a reaction in the body) responsible for the physiological effects. Some studies have undertaken several methods of extraction to determine the chemical makeup of kambó and to test the effects of each peptide that is present in large amounts.

Phyllocaerulein is present in the highest concentration and seems to be responsible for kambó's principal effects. It has a strong effect on the gastrointestinal smooth muscle, stimulating its motility, bile flow, pancreatic and gastric secretions, and mediates analgesic effects in the central nervous system.

Phillokinin has hypotensive effects on the cardiovascular system.

Phyllomedusin has also strong hypotensive effects, stimulates gut motility (contributing to purging), lacrimal, and salivary secretions.

Sauvagine causes a fall in blood pressure due to a vasodilatation of mesenteric vascular area and provokes intense tachycardia. In the central nervous system, it seems to activate the pituitary-adrenal axis, increasing levels of corticosterone, catecholamines (such as adrenaline) and glucose in plasma.

Opioid peptides. Ala-Deltorphin and Lys7-Dermorphin have strong affinity for opioid receptors, surpassing that of morphine. This is one of the reasons the effect of the venom has been generally attributed to these substances. However, the amounts present in Kambó are so limited that they seem to have no significant biological activity in humans.

Peptides from the **dermaseptin** family have been detected in reduced amounts. These are described to inhibit the growth of a broad spectrum of microorganisms (protozoa, fungi, bacteria and viruses) without harming differentiated mammalian cells, thus being responsible for a potential antibiotic activity.

As previously mentioned, dosage is measured by the number of dots applied, each dot contains approximately 10mg of skin secretion with a rough measure of 5 mm in diameter (size of a green pea). Dose of choice will depend on body size, experience, and reasons for application, or on the practitioner's tradition.

» Low dose: 1 to 3 dots
» Average dose: 3 to 10 dots
» High dose: More than 10 dots

Matses indigenous people from southwestern Amazon have traditionally used Kambó application as additional support for hunting practices. They self-apply up to 20 to 30mg of Kambó twice daily.

Some traditional practitioners may reach 100 dots in a single application, yet this dose is limited to cultural rituals and experienced users. It would be dangerous for an unexperienced user to apply a very high dose..

EFFECTS

The principal effects of Kambó use seem to correspond to the peptides present in larger amounts, affecting the vascular system, glandular secretions, gastrointestinal activity and regulation of the pituitary-adrenal axis in the central nervous system.

Many other peptides are present in lesser quantities, though their roles in producing effects are uncertain. In humans, it is unlikely that their presence has significant effects due to their very reduced amounts. However, this possibility cannot be excluded. One possibility is that some of these peptides may act together to cause a slight increase of vasodilatation and permeability in the blood-brain barrier, facilitating the compounds access into the circulator system and the central nervous system, but this is still unclear.

By applying it in a fresh wound, Kambó can be absorbed subcutaneously and enter the circulatory system. Within few minutes, a rather unpleasant acute physiological response manifests, generally characterized by an increase of the heart rate (that can reach the 190bpm), a dramatic rise or fall in blood pressure, sweating, dizziness, and may include nausea and vomiting and/or defecation. The acute effect is described to last for several minutes before usually fading away within 5 to 20 min. Other more variable effects in the acute phase may include a feel of strong pressure in the head, neck and chest, stomach pain, inflammation of the throat, blurred vision, dry mouth, a sense of bodily heaviness (difficulty moving), and also a numb and swollen tongue, lips, and face (some users report in the acute symptoms to actually

feel like a toad).

When acute effects are fading away, a strong sense of fatigue and sleepiness may appear, in which case it may be necessary to rest.

A large amount of liquid is consumed before Kambó application takes place, usually two litters of water, to help with the purging process.

Positive effects of Kambó use are described by users several hours (24h) after the acute effects subside. Users report being left with a sensation of strength, increased sensorial awareness, and mental clarity, as well as strengthening of the immune system.

LEGAL STATUS

Currently there is no legislation regulating the use of Kambó.

The only legal measure over the use of Kambó to this date is a 2004 ban from the Brazilian government of its commercialization and advertising.

The increasing popularity of Kambó has started a debate on who is the rightful owner of the knowledge surrounding its use. Its origins are generally linked to the indigenous people of South West Amazon and one of the main concerns and topics for debate concerning kambo is that of 'biopiracy' – the notion that resources located in a territory or practices originating among indigenous people are being stolen. The increasing availability and interest in kambó as an alternative medicine practice is attracting the attention of those who want to explore its therapeutic potential, as well as by those interested in profiting from it, as it can be regarded in some cultures as an "emerging market." This was the main reason for the legal measure taken following complaints from traditional Kambó using tribes.

PREVALENCE OF USE

There is little information on the prevalence of use of Kambó in western countries. Although its use had always been associated with neo-shamanic practices in communities that use ayahuasca, it had never been very widespread nor well-known. This situation has changed over the last five years, and especially during 2017-2018. Now, Kambó is more well-known and popular, and there are many neo-shamanic retreats in which Kambó is used along other ethnobotanicals such as ayahuasca, rapé and *Bufo alvarius*. Numbers are still uncertain as there is no data or research about the prevalence of use, but the general impression is that Kambó is becoming an increasingly used substance.

HEALTH AND RISK REDUCTION

Kambó affects mainly the circulatory system, in which case its application wouldn't be recommended specially for persons with a clinical history of high blood pressure or heart disease.

Some reports have been published on Kambó's toxicity, i.e. a hepatitis case related to the use of the frog's venom. There is a forensic report of a sudden death which happened 30 minutes after applying Kambó. In this report, they indicate that this person was habitually using Kambó and that an acute reaction accumulated over a continued use might have been the cause of death.

Accident reports related to Kambó use are caused mainly by lack of information. Some cases of hyponatremia have been reported due to an excessive amount of water intake. Six to 10 liters of water consumed in a short period of time can greatly lower the concentration of electrolytes in blood stream, which can pose a threat for the physiological stability of the organism and it's live. In these cases, users were overwhelmed by the experience induced by the Kambó application and tried to deal with it by drinking excessive amounts of water.

There is currently no clinical research concerning Kambó, there is very little published information on the topic is registered, and its popularity is rather recent. Thus, the actual benefits are yet to be established.

Medical doctors who are aware of it maintain a cautious attitude. It is difficult to predict how a person with neurologic or heart problems or other conditions could be affected by the application.

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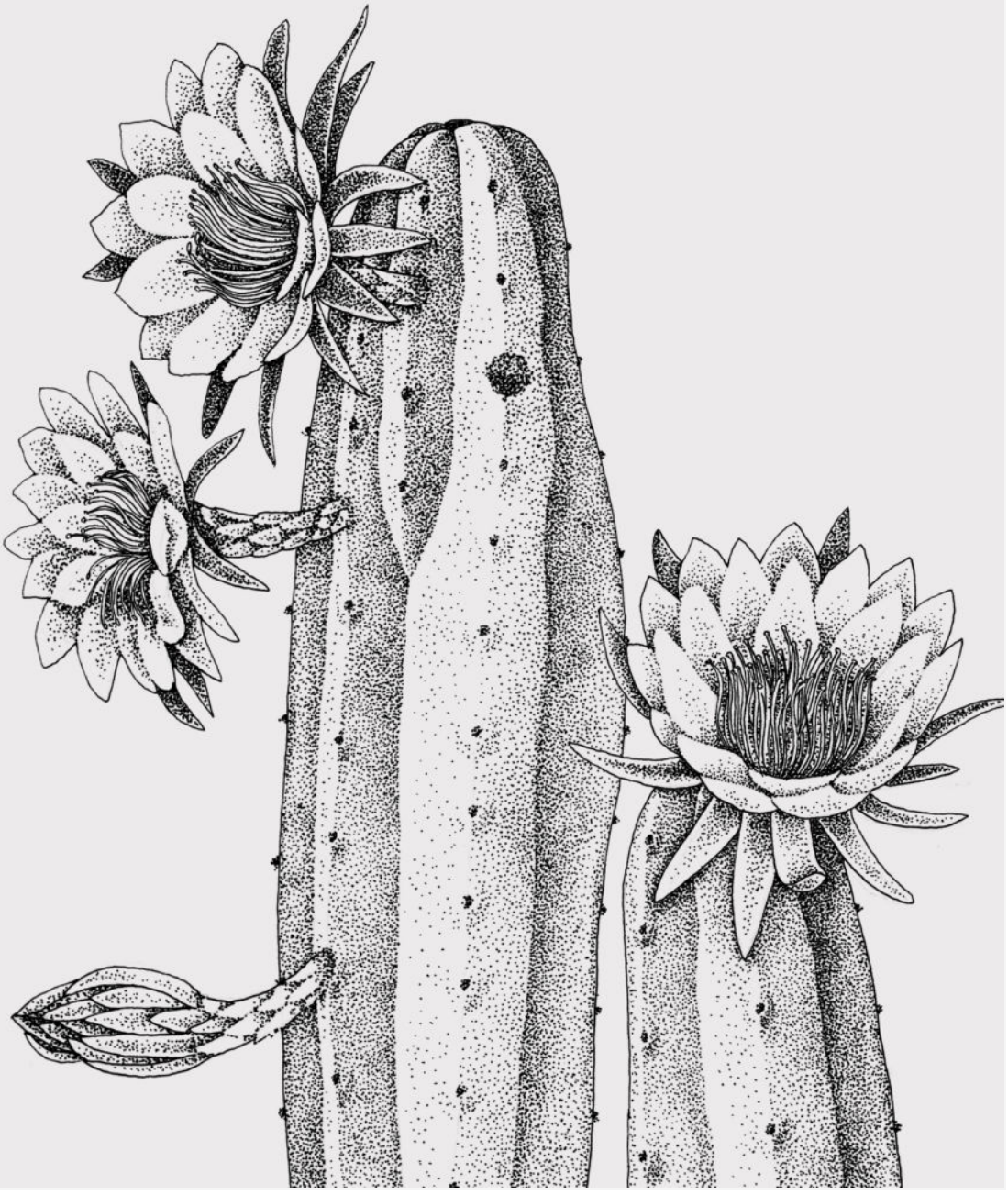
SAN PEDRO



SAN PEDRO

Echinopsis pachanoi is a cactus native to South America, with traditional religious and medicinal uses spanning more than 3000 years. Out of the various alkaloids it contains, mescaline is responsible for its psychoactive effects.

BASIC INFO

San Pedro is a columnar cactus traditionally used for medical and religious purposes in certain parts of South America. Other cactus species that belong to the botanical genus *Echinopsis* (formerly called *Trichocereus*) are also known by this name, mainly *Echinopsis pachanoi* and *Echinopsis peruviana*, although there are other varieties such as *E.puquiensis, E.santaensis*, and *E.schoenii.*

San Pedro contains different alkaloids, including mescaline, a substance with psychoactive effects.

In traditional cultures it is known by different names, such as huachuma, achuma, wachuma, and aguacolla.

ORIGIN / HISTORY

The earliest evidence San Pedro use has been found in Peru, in the Guitarrero cave of the Callejón de Huaylas valley. Fossil remains of the cactus dating from 6800-6200 BCE have been found in these caves, including the presence of samples from different eras. Thus, the use of *E. pachanoi* is among the oldest of the different ancestral psychoactive plants.

At the Chavín de Huantar site, representations of San Pedro cactus engraved in stone have been found, along with textiles and ceramics, which suggest that its use was already understood and practiced. These objects date from the year 1300 BCE. Ceramics have also been found with representations of the cactus and archaeological evidence of the use of San Pedro in the Nazca, Cupisnique (1500 BCE) Chimú, Lambayeque (750-1350 CE) and Moche (100-750 CE) cultures has been discovered, along with the Chavín. It has been suggested that between 200 BCE and 600 CE *E. Pachanoi* was domesticated and was being cultivated on the Peruvian coast.

The ongoing use of San Pedro until the Spanish colonial period can be deduced from the writings of the conquistadors describing San Pedro's effects when ingested by native peoples, and from archaeological evidence. Just as they did with mushrooms and peyote, the conquistadors and the Catholic Church fought against the religious use of *E. pachanoi.*

Later, Christianity influenced indigenous ritual practices and *E. pachanoi* was named San Pedro and used in a syncretic way, blending traditional elements with Christian ones.

Thus, the San Pedro ceremony has existed for more than 3,000 years and possibly up to about 8,000.

Traditional use today

In Andean medicine, San Pedro continues to be used by different ethnic groups in Peru and Ecuador, such as the Saraguro, a group belonging to the Kichwa in Ecuador. Members of the community who know how to use medicinal and hallucinogenic plants are known as Yachakkuna, and the medical system of these communities is a blend of ancestral indigenous knowledge and modern medical methods. San Pedro is one of the therapeutic tools available, although many other plants and techniques are also used. San Pedro is considered a protector of families, marriage, and peaceful coexistence among family members, and for this reason it is usually cultivated close to homes.

The main use of San Pedro is for diagnostic reasons – the healer ingests San Pedro to be able to see the nature of the patient's illness. Other uses include purification of the organism through purging, since the ingestion of the San Pedro decoction can produce vomiting and diarrhea, and

as an anti-inflammatory in the form of a topical poultice.

The San Pedro ritual is known as a mesa, and it is done with the purpose of healing a sick person for whom normal treatment has not worked, or to obtain money, recover one's lover or find lost objects or animals. A mesa consists of a set of objects that the healer has collected over time and that may include swords or machetes, staffs, stones, shells, the San Pedro preparation, sugar, tobacco, brandy, candles and other elements. These objects confer power to the healer.

CHEMICAL COMPOSITION AND DOSAGE

Mescaline is the primary alkaloid of the San Pedro cactus and hordenine, lophophine, DMPEA (3,4-Dimethoxyphenethylamine), and lobivine have also been detected.

Mescaline is mostly concentrated in the green skin of the outer part of the cactus (called chlorenchyma), and the concentration of this alkaloid can vary greatly depending on the species and the specimen. Some analyses have found concentrations ranging from 0.053% to 4.7% of the total weight of the cactus. Thus the amount of San Pedro needed to induce psychoactive effects can vary considerably.

In the past, it was believed that *E. peruvianus* was much more potent than *E. pachanoi,* however, taking into account more recent analyses and a broad review of the different studies, this difference is not confirmed and it seems that the mescaline concentration in both species is very similar.

Dosage of mescaline:

The active dose of oral mescaline hydrochloride is between 150 and 700 milligrams. Customary doses of mescaline have been calculated based on 3.75mg/kg of weight.

» Threshold dose: 100mg
» Low dose: 100 – 200mg
» Average dose: 200 – 300mg
» High dose: 300 – 500mg

Some analyses of traditional preparations have found doses ranging from 34mg to 159mg of total alkaloids, a relatively low and barely psychoactive amount. It appears that patients who receive traditional treatments with San Pedro ingest sub-psychoactive doses and do not experience psychedelic effects..

EFFECTS

The effects of *E. pachanoi* are mainly due to the alkaloids it contains, in particular mescaline. The alkaloid content is similar to that of peyote, and therefore the subjective effects are similar as well.

San Pedro preparations tend to have a bitter and unpleasant taste, it is therefore not uncommon for nausea and vomiting to occur after ingestion, although mescaline itself may be the cause of some of these effects.

The psychological effects of San Pedro are usually described as being similar to those of peyote and mescaline, although the doses used traditionally do not seem to be high enough to produce a psychoactive experience. However, neo-shamanic groups use higher doses of San Pedro, so the effects that occur are similar to those produced by "classical psychedelics," such as LSD and psilocybin. These include:

» Visions with eyes open and closed
» Deep change in cognition, perception, and consciousness
» Insightful psychological experiences
» Spiritual experiences
» Changes in the perception of time and space

Difficult experiences can occur, occasionally including anxiety and distress, although they seem to be less frequent than with other plants and substances.

Mescaline has a mildly stimulating effect, although some traditional reports speak of an initial state of lethargy after ingesting San Pedro

SAN PEDRO

LEGAL STATUS

Mescaline, the psychoactive alkaloid of San Pedro, is a substance controlled by the 1971 Vienna Convention and is listed in Schedule I. It is therefore considered a substance whose use, sale and manufacture are prohibited. However, the San Pedro cactus is not included on the list of scheduled substances and its regulation depends on the legislation of each country.

For example, in Canada mescaline is on the Schedule III list and peyote (another cactus containing mescaline) is explicitly exempt from regulation if it is not prepared for ingestion, while in Switzerland, San Pedro is considered illegal. Other countries, such as Spain, do not mention peyote on their lists of controlled plants, although this does not imply that the sale of peyote is legal.

In most countries, the cultivation of San Pedro cactus is not prosecuted, while preparations, decoctions or extractions made for human consumption may be.

PREVALENCE OF USE

Mescaline is an alkaloid that has been relatively well-known since the 1950s. Even so, the prevalence of consumption of mescaline has always been low, and the cacti that contain it are plants with very limited use compared to other traditionally-used psychoactive plants. The synthesis of mescaline or its extraction is more expensive, complicated, and less efficient in economic terms than that of other substances, so mescaline has not usually been offered on the black market, although some substances, such as LSD, have been sold in this way.

Unlike peyote, San Pedro grows rapidly, so it is not an endangered species and self-cultivation is much easier. Still, the use of San Pedro is very limited compared to other plants.

In the 2017 Global Drug Survey, mescaline does not even appear among the substances published in the report. In the survey carried out for the Psychēplants, out of a total of 593 users of psychoactive plants, 148 responded that they had used San Pedro; approximately 25%. This percentage is higher than less common plants such as khat, kratom, *Argireya nervosa*, the Daturas, *Bufo alvarius*, iboga and peyote, but lower than ayahuasca, psilocybin mushrooms and *Salvia divinorum.*

HEALTH AND REDUCTION RISK

The health and risk reduction concerns that must be taken into account when using San Pedro are equivalent to those that should be considered when using peyote, and to some extent, any other classical psychedelic, such as LSD or psilocybin mushrooms.

Physical health

Due to the possibility of intense experiences that may generate anxiety, people with a history of cardiovascular diseases should refrain from using San Pedro, particularly those who are taking medication to control these pathologies and who have medical conditions for which reduced amounts of physical activity have been indicated.

San Pedro has slightly stimulating effects, so it should not be combined with other stimulating substances.

Psychological Health

As with any psychedelic substance, it is extremely important to consider three factors when it comes to reducing the risks associated with its use: the dose, the set (prior mental state) and the setting (the context in which it is used).

With regards to dosing, it is important to be aware that the effects of mescaline and San Pedro can take up to two hours to appear, so one could make the mistake of believing that the dose was insufficient, re-administer, and ultimately take too high a dose. It is important to calculate the dose in advance and wait a sufficient period of time before deciding to increase the dose.

As with any classical psychedelic, the effects of mescaline

and San Pedro depend, to a large extent, on the mental state of the person who takes it. Some researchers have called psychedelics "nonspecific amplifiers of consciousness," so their effects can be extremely variable from person to person, as well as on varying occasions. Therefore, caution must be taken when using San Pedro in situations of stress, depression, worry, or when experiencing life difficulties. In addition, the effects depend on the context in which these substances are used, as well as the company and the physical environment. For this reason, it is important to carefully plan the way in which San Pedro is going to be used.

People with a history of psychiatric conditions such as psychotic disorders, bipolar disorder, suicidal thoughts and others should refrain from using mescaline if it is not in a clinical context, as there is a risk of increased symptoms and decompensation.

As with any psychedelic substance, unconscious content may emerge during an experience with San Pedro. These processes can be emotionally intense and sometimes involve feelings of fear, distress and difficulty, in much the same way that they can cause experiences of joy and ecstasy. For this reason, it is usually recommended to have an open and accepting attitude towards the content of the experience.

Forms of use

Currently, San Pedro is used in a variety of contexts, from the most traditional settings in San Pedro mesas in Peru and Ecuador, to Western neo-shamanic contexts.

There are different ways of preparing San Pedro according to the intended purposes and the tradition in which it is used. Different forms of administration have been utilized in traditional cultures, from decoctions that are ingested and generally contain low doses of mescaline, to poultices to treat dermatological conditions, inflammation and pain, to San Pedro powder mixed with other plants, such as tobacco, and used intranasally.

Decoctions generally use either the entire chopped cactus or parts of it. The powder from the outer green skin of the cactus can also be ingested, as this is where the majority of mescaline is concentrated.

In psychonautic contexts, extractions of pulverized bark have been used to reduce the amount of plant material that one must consume.

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