

# **PSILOCYBIN GUIDE**



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# What is Psilocybin?

Psilocybin is a naturally occurring psychedelic compound found in over 200 species of mushrooms, often referred to as 'magic mushrooms', primarily belonging to the *Psilocybe* genus.<sup>1</sup> Psilocybin metabolizes into psilocin, a chemical that binds to serotonin receptors in the brain, triggering hallucinations and introspection.<sup>2</sup> In 1956, Roger Heim identified a psychoactive mushroom originating in Mexico as *Psilocybe*, and in 1958, Swiss Chemist Albert Hofmann, who also discovered lysergic acid diethylamide (LSD), first identified psilocybin and psilocin as the active compounds in these mushrooms.<sup>3</sup>

For centuries, psychedelic compounds, including these mushrooms, have held a prominent role in various cultures for their hallucinogenic and spiritual properties.<sup>4</sup> In recent years, the field of psychedelic research has gained significant interest, exploring the potential therapeutic uses of psilocybin and related compounds in the treatment of both mental and physical health conditions.

This renaissance of psychedelic research in recent years has revealed numerous potential therapeutic applications for psilocybin. Clinical studies in the United States and from around the world have shown promising results in the treatment of various mental health issues, including depression,<sup>5</sup> anxiety,<sup>6</sup> addiction,<sup>7</sup> and post-traumatic stress disorder (PTSD).<sup>8</sup> Outside of clinical settings, a recent large-scale naturalistic study of psilocybin conducted by researchers at Unlimited Sciences, Johns Hopkins University, and Ohio State University found naturalistic psilocybin use is highly consistent with results from a growing body of clinical trials, including lasting improvements in mental health symptoms related to anxiety, depression, and substance misuse. Research is currently proposed or ongoing into psilocybin's effects on a number of physical health conditions as well, including migraine headache, cluster headache, chronic pain, cancer pain, functional neurological disorder, and post-treatment Lyme disease.

# Use of Psilocybin Through the Ages

Different cultures (e.g., Olmec, Zapotec, Maya, and Aztec) have used psychoactive mushrooms for spiritual practices for thousands of years across different regions and societies around the world.<sup>9</sup> Historical records, archaeological evidence, and academic articles allude to its use for religious, spiritual, and medicinal purposes. Psychedelic Singh, Gaughen, Hill, Morski, & Lowe. Psilocybin Guide. Page 5 of 38

substances, including psilocybin, have been recognized as a key component of religious and spiritual practices among several indigenous cultures.<sup>4</sup> These substances are often used to facilitate communication with deities or ancestral spirits, allowing individuals to seek self-knowledge and healing, and providing opportunities for personal growth and transcendence.<sup>10</sup>

The earliest known evidence of ritualistic use of psilocybin dates back 6,000 years to the ancient Tassili n'Ajjer civilization in present-day Algeria.<sup>11</sup> Indigenous cultures, such as Native Mexican and Guatemalan groups, have long integrated psilocybin mushrooms into their spiritual and medicinal practices. Their use is often linked with divination, communication with ancestors, and connecting with the spirit world.<sup>12</sup> For example, the Mazatecs of Oaxaca, Mexico, use psilocybin mushrooms as a tool for healing and self-discovery.<sup>10</sup> The mushrooms are often consumed in rituals supervised by experienced guides, who guide the participants through the process and interpret their experiences.

Ignited largely by the works of R. Gordon Wasson and researchers like Timothy Leary, the 20th century has seen a resurgence of interest in the use of psilocybin. Psilocybin has been utilized in modern contexts for personal growth, spiritual exploration, and as an adjunct to psychotherapy. Recent scientific research has explored the potential therapeutic benefits of psilocybin for a variety of mental health issues, further driving interest in its psycho-spiritual applications.

A growing number of people are participating in ceremonies that incorporate the traditional elements of indigenous practices, led by experienced facilitators in various settings. Additionally, certain religious groups, such as the Native American Church, have integrated psilocybin along with other entheogens into their religious practices.<sup>13</sup>

# How is Psilocybin Used in Modern Medicine and Research

In recent years, there has been growing interest in the use of psilocybin in modern medicine and research. While psilocybin has long been used for spiritual and recreational purposes, more and more research is being conducted on the potential medical benefits of psilocybin.

One of the most promising areas of research for psilocybin is its potential use as a treatment for various mental health conditions. Following a long hiatus stemming from a restrictive regulated drug schedule, the investigation of psychedelic compounds has reemerged with increased focus on potential applications of psychedelics in the treatment of mental health conditions.<sup>14</sup> In 2018 the Food and Drug Administration (FDA) granted breakthrough therapy status to psilocybin for treatment-resistant depression.

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# The Potential Therapeutic Uses of Psilocybin

### Depression, anxiety, and PTSD

One of the most promising areas of research for psilocybin is its potential to treat mental health conditions such as depression, anxiety, and PTSD. Studies have shown that a single dose of psilocybin can lead to significant improvements in mood and decrease symptoms of treatment-resistant depression as compared to a placebo.<sup>15</sup> A recent study reported that the effects of psilocybin-assisted therapy lasted up to twelve months after the initial dose.<sup>16</sup> A recent meta-analysis of the effects of psilocybin found significant improvements in depression and anxiety symptoms<sup>17</sup> while another study showed the clinical utility of treating symptoms of obsessive-compulsive disorder with psilocybin.<sup>18</sup> A recent review on the use of psychedelics for the treatment of PTSD concluded that psychedelics offer a promising new approach for this chronic illness that is associated with high rates of comorbid psychiatric and medical issues.<sup>19</sup> Outside of controlled research settings, naturalistic use of psilocybin has shown consistent results with clinical trials. Unlimited Sciences' prospective longitudinal data collected before and after a planned psilocybin experience outside of clinical settings showed persisting reductions in anxiety and depression.<sup>39</sup>

## Substance abuse and addiction treatment

Psilocybin has also shown promise in the treatment of substance abuse disorders. Studies have shown that participants with alcohol use disorder who received even a single dose of psilocybin had reduced cravings and increased abstinence rates compared to those who received a placebo.<sup>7,20</sup> Consistent with these results, Unlimited Sciences' naturalistic research study on psilocybin use found significantly decreased alcohol misuse persisting for months after psilocybin ingestion.<sup>39</sup> Other studies have found that psilocybin-assisted therapy was effective in decreasing nicotine dependence<sup>21</sup> and that 60% of participants remained smoking abstinent after a mean of 30 months.<sup>22</sup> These results suggest that psilocybin may have a role to play in treating various types of addiction.

### End-of-life distress

In addition to its potential for treating mental health conditions, psilocybin has also been studied as a treatment for end-of-life distress. One study showed that a single dose of psilocybin can lead to sustained improvements in satisfaction with life and mindfulness-related capacities in individuals facing terminal illness.<sup>23</sup> This is further supported by a randomized double-blind trial which found substantial and sustained decreases in depression and anxiety among patients with life-threatening cancer after receiving psilocybin-assisted therapy.

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# Psychopharmacology of Psilocybin

When ingested, psilocybin is converted into a compound called psilocin. Psilocin then binds to serotonin receptors in the brain, specifically the 5-HT2A receptor.<sup>24</sup> This binding triggers a series of chemical and electrical reactions that result in altered perception, thought processes, and mood. These effects can last for several hours.

A drug's pharmacodynamics can be affected by physiologic changes due to:

- A disorder or disease
- The aging process
- The presence of other drugs

### Absorption

The absorption of psilocybin occurs primarily in the gastrointestinal tract. After ingestion, it is broken down by enzymes in the body into its active form, psilocin.<sup>25</sup> This process can take anywhere from 30 minutes to an hour, depending on various factors such as dosage and individual metabolism. Once in its active form, psilocin can easily cross the blood-brain barrier, leading to its psychoactive effects.<sup>26</sup>

### **Distribution and Metabolism**

Once absorbed, psilocin is distributed throughout the body via the bloodstream. It then undergoes metabolism in the liver before being eliminated from the body. The exact process of metabolism is not yet fully understood. However, it is believed that liver enzymes break down psilocin into inactive forms. This process can take several hours, during which time an individual may experience a prolonged altered state of consciousness.<sup>27</sup>

### **Elimination and Half-Life**

The elimination of psilocin and its metabolites from the body occurs primarily through urine.<sup>26</sup> However, a small percentage may also be eliminated through breath and sweat.

The half-life of psilocybin, the time it takes for half of the compound to be eliminated from the body, is approximately 160 minutes, while that of psilocin is around 50 minutes.<sup>26</sup> This means that after about six to eight hours, most traces of psilocybin are no longer detectable in the body. A drug is considered fully eliminated after 5 half-lives.

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# Chemistry and forms of psilocybin

Psilocybin (O-phosphoryl-4-hydroxy-N, N-dimethyltryptamine) is a prodrug for the psychoactive compound psilocin (4-hydroxy-N, N-dimethyltryptamine).<sup>26</sup> A prodrug is a pharmacologically inactive medication or compound that, after intake, is metabolized, (meaning converted within the body) into a pharmacologically active drug. When ingested, psilocybin is converted to psilocin, which is responsible for the psychoactive effects. Psilocybin-containing mushrooms typically show variations in psilocybin and psilocin concentrations depending on factors like species, growth conditions, and preservation methods.<sup>25</sup>

Psilocybin can be found in several different forms, each with varying potencies and effects. Here are some common forms:

- Raw mushrooms: The most natural form of psilocybin, typically consumed by ingesting dried magic mushrooms.
- Psilocybin extract: A concentrated form of the compound, created by extracting the psilocybin from the mushrooms.
- Psilocybin truffles: Also known as "philosopher's stones," these are underground fungal growths that contain psilocybin.
- Psilocybin edibles: Psilocybin can be infused into food or beverages, making it more palatable for consumption.
- Synthetic psilocybin: Chemically developed in a laboratory, allowing for precise dosing and purity.

### Neurotransmitters involved

Psilocybin primarily targets the serotonin system, which is involved in regulating mood, behavior, and cognition. Specifically, psilocybin binds to serotonin receptors (5-HT2A) and activates them, leading to changes in brain activity and perception.<sup>24</sup>

In addition to targeting serotonin, psilocybin also affects other neurotransmitters such as dopamine and glutamate.<sup>28</sup> Dopamine is known for its role in reward and motivation. Psilocybin has been found to increase dopamine levels in certain areas of the brain. This effect may explain why some users report feelings of euphoria and heightened creativity while under the influence of psilocybin. Glutamate, on the other hand, is involved in learning and memory. Psilocybin has been shown to disrupt glutamate signaling in certain brain regions, which could contribute to its hallucinogenic effects.

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It is important to note that psilocybin's effects on neurotransmitters are not fully understood yet. As mentioned earlier, research is still ongoing, and much remains to be discovered about this compound and its potential therapeutic uses.

#### Potential pathways/mechanism of action

#### Serotonin receptor interaction

Psilocybin is known to mimic the actions of serotonin, a neurotransmitter that regulates mood, cognition, and perception by primarily binding to the serotonin 2A receptor (5-HT2A), leading to alterations in brain activity and changes in perception.<sup>29</sup> The activation of these receptors may also promote neuroplasticity, which is the ability of the brain to adapt and form new connections.<sup>24</sup> This could potentially explain why psilocybin has been shown to have long-lasting effects on behavior and thought patterns.

#### Default mode network

The default mode network (DMN) is a group of brain regions that is active when an individual is at rest or not focused on a particular task. Studies have shown that psilocybin may decrease activity in the DMN, leading to a state of decreased self-awareness and ego dissolution.<sup>30</sup> This reduction in activity may also explain why individuals report feeling more connected and empathetic toward others after taking psilocybin. Further, it has been hypothesized that decreased activity in the DMN may allow for increased introspection and self-reflection, which could be beneficial for individuals struggling with mental health disorders.<sup>31</sup>

#### Neuroplasticity

As mentioned earlier, psilocybin has been found to promote neuroplasticity in the brain. This means that psilocybin can facilitate the growth of new neurons and connections between them, leading to changes in brain function and behavior.<sup>32</sup> Studies have also shown that psilocybin may increase levels of brain-derived neurotrophic factor (BDNF), a protein that plays a crucial role in promoting neuroplasticity.<sup>33,34</sup> These findings suggest that psilocybin may have potential therapeutic effects on conditions such as depression and anxiety, which are often associated with reduced BDNF levels.

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### **Tolerance to psilocybin**

Tolerance refers to the body's natural response to repeated exposure to a substance. In the case of psilocybin, this means that with continued use, the effects of the compound may become less intense or even non-existent.<sup>35</sup> As with research on psilocybin's therapeutic effects, the research on the tolerance to psilocybin is also in its early stages.

Although the exact mechanisms behind psilocybin tolerance are not fully understood, tolerance generally occurs with repeated dosing and is thought to be due to down-regulation of 5HT<sub>2A</sub> receptors.<sup>35</sup> However, it is believed that repeated activation of certain receptors in the brain leads to desensitization, making them less responsive to the compound's effects.<sup>36</sup> There may also be cross-tolerance between LSD and psilocybin.<sup>35</sup> Psilocybin, like other hallucinogens, is not known to cause dependence, craving, or withdrawal.

#### What are the effects of tolerance?

Tolerance can have significant implications for those using psilocybin for therapeutic purposes. It can lead to a decrease in the intensity of experiences, making it less effective for treating certain conditions.

#### How long before tolerance develops?

The duration of tolerance to psilocybin varies from person to person. A study in mice found it could develop after one use.<sup>36</sup>

#### **Managing tolerance**

As with any substance, it is essential to approach the use of psilocybin with caution and respect. To manage tolerance, it is recommended to follow a moderate and responsible dosing schedule, avoid frequent use, and take breaks from usage to allow for tolerance to decrease.

Some studies have shown promising results with intermittent dosing schedules and combination therapies.<sup>37</sup> Intermittent dosing involves taking breaks between doses of psilocybin to prevent or reduce the development of tolerance. This method has been used in traditional shamanic practices and has been suggested as a potential strategy for maintaining the long-term benefits of psilocybin therapy.<sup>38</sup>

It is crucial to consult with a healthcare professional before using psilocybin for therapeutic purposes. A professional can help monitor your dosage and provide

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guidance on managing tolerance while also ensuring the safe and proper use of this substance.

# Different types of psilocybin mushrooms

There are over 200 different species of psilocybin mushrooms found all around the world, each with its own unique appearance and effects. While there are many different types of psilocybin mushrooms, they all contain the same psychoactive compounds and have similar effects. However, each species has its own unique characteristics and potency, making them popular choices for different purposes. Some of the most common types of psilocybin mushrooms and their characteristics are:

• Psilocybe Cubensis

The *Psilocybe Cubensis* is the most well-known and widely available species of psilocybin mushroom. It can be found growing naturally in tropical and subtropical regions but is also cultivated in many other parts of the world. This mushroom typically has a golden or caramel-colored cap with white spots and a long stem.

• Psilocybe Semilanceata

Also known as the "liberty cap", *Psilocybe Semilanceata* is a small, brown mushroom found in grassy fields and meadows. It is commonly found in Europe and North America. This species has a distinct pointed cap with a nipple-like appearance.

• Psilocybe Mexicana

As the name suggests, *Psilocybe Mexicana* is found primarily in Mexico and Central America. It has a unique appearance with a bell-shaped cap and a tall, thin stem.

• Psilocybe Cyanescens

Native to the Pacific Northwest region of North America, *Psilocybe Cyanescens* or "wavy caps" are known for their wavy caps and potent effects. They can also be found in other parts of the world, such as Europe and New Zealand.

• Psilocybe Azurescens

Considered one of the most potent species of psilocybin mushrooms, *Psilocybe Azurescens* is also found in the Pacific Northwest region of North America. It has a unique appearance with a caramel-colored cap and thick stem.

• Other known species of psilocybin-containing mushrooms include:

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- o Psilocybe Antioquiensis
- o Psilocybe Atlantis
- o Psilocybe Australiana
- o Psilocybe Aztecorum
- o Psilocybe Caerulescens
- o Psilocybe Caerulipes
- o Psilocybe Cyanofibrillosa
- o Psilocybe Fimetaria
- o Psilocybe Heimii
- o Psilocybe Liniformans
- o Psilocybe Medullosa
- o Psilocybe Moravica
- o Psilocybe Natalensis
- o Psilocybe Ovoideocystidiata
- o Psilocybe Pelliculosa
- o Psilocybe Samuiensis
- o Psilocybe Serbica (bohemica)
- o Psilocybe Silvatica
- o Psilocybe Strictipes
- o Psilocybe Stuntzii
- o Psilocybe Subcubensis
- o Psilocybe Tampanensis
- o Conocybe Cyanopus
- o Conocybe Kehneriana
- o Conocybe Siligineoides
- o Conocybe Smithii
- o Inocybe Aeruginascens
- o Inocybe Coelestium
- o Inocybe Haemacta
- o Inocybe Tricolor
- o Panaeolus Bisporus
- o Panaeolus Cambodginiensis
- o Panaeolus Cyanescens
- o Panaeolus Tropicalis
- o Pluteus Brunneidiscus
- o Pluteus Cyanopus
- o Pluteus Glaucus
- o Pluteus Nigroviridis
- o Pluteus Salicinus
- o Pluteus Villosus
- o Pluteus Phaeocyanopus

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# **Psilocybin Consumption**

#### Method of administration

Oral administration is the only widely available method for consuming psilocybin. This involves ingesting the dried or fresh mushrooms directly or in the form of tea. The effects usually begin within 20-30 minutes after ingestion and can last for up to six hours. The potency and effects of psilocybin can vary greatly depending on the type of mushrooms and individual factors such as metabolism.<sup>27</sup> Additionally, psilocybin can cause nausea and vomiting when ingested orally, making it less desirable for some people.

#### Dosing

#### Microdose

#### <u>Click here for a full data-driven quide to microdosing which can be found on our</u> <u>Unlimited Sciences blog.</u>

Microdosing refers to the practice of regularly or semi-regularly consuming low doses of psychoactive substances. Dozens of studies have examined the effects of microdosing, reporting a wide variety of motives for microdosing psychedelics, including performance enhancement, mood enhancement, curiosity, treatment of health conditions, self-fulfillment, coping with negative situations, increasing social connection, improving mental health, personal or spiritual development, and enhancing cognitive performance. Participants generally report confidence that microdosing fulfilled these aims, and even indicate that microdosing is being used as an alternative to conventional medicines for mental and physical health issues. However, there is currently little clinical evidence to support the benefits of microdosing.

The goal of microdosing is not to produce noticeable or profound changes in cognition and perception. Data from recent systematic reviews on low-dose psychedelics by Vince Polito and Paul Liknaitzky (2022), and Joseph Rootman and colleagues (2021) summarizes microdose quantities used in past research. As an estimate, a microdose is between approximately one tenth and one twentieth of a typical recreational dose. Since an effective recreational dose can vary substantially from one individual to the next, use a conservative "low and slow" approach and start as low as possible as you identify an appropriate dose, especially if you aren't sure of how much you're giving yourself. Track your progress carefully and accurately through written records. Polito and Liknaitzky,

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and Rootman and colleagues, provide the following plausible dose ranges for microdoses of different substances based on previous research:

*Psilocybe cubensis* dried mushroom, oral ingestion: 0.1-0.5g/70kg (per 70kg bodyweight); Low dose  $\leq 0.1g$ ; Medium dose = 0.1-0.3g; High dose  $\geq 0.3g$ .

#### Macrodose

Regular doses (as opposed to microdoses) will come with a range of perceptual changes, which vary widely from individual to individual. Even at high doses, psilocybin is reported to have the most favourable safety profile of all psychedelic drugs, and thousands of years of anecdotal evidence in addition to modern-day scientific studies confirm that psilocybin has low physiological toxicity, low abuse/addictive liability, safe psychological responses, no associated persisting adverse physiological or psychological effects during or after use.<sup>28</sup>

Various species of psilocybin mushrooms exhibit significant variation in potency, influenced by factors such as species or variety, origin, growing conditions, and age. For instance, Psilocybe cubensis and Psilocybe semilanceata, commonly known as liberty caps, typically contain 10 mg of psilocybin per gram of dried mushroom weight (1% w/w). Some other species, such as Psilocybe azurenscens and Psilocybe bohemica, may contain slightly higher concentrations of psilocybin. The typical dose of psilocybin required to induce hallucinogenic effects ranges from 4 to 10 mg (Beck et al., 1998) or 50 to 300  $\mu$ g/kg body weight (Hasler et al., 2004). Therefore, the minimum amount of mushrooms needed to achieve the desired recreational effect is approximately 1 gram of dried magic mushrooms or 10 grams of fresh magic mushrooms.

Reports from <u>Erowid</u> indicate that Common dosing for recreational use is reportedly somewhat higher, ranging between 1 and 3.5 to 5 grams of dried mushrooms or 10 to 50 grams for fresh mushrooms (Erowid, 2006). However, these dosage ranges should be interpreted cautiously due to the difficulty in accurately estimating the concentration of the active hallucinogenic substances, such as psilocybin, within mushrooms. Additionally, besides psilocybin and psilocin, magic mushrooms may contain other pharmacologically active compounds like indoles, phenylethylamines, and baeocystin.

It's worth noting that short-term tolerance can develop rapidly to both the physical and psychological effects of psilocybin, potentially necessitating increased dosages to achieve the desired effect.

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From our own research at Unlimited Sciences on naturalistic psilocybin use, among individuals who reported a dosage of dried, whole psilocybin mushrooms in grams, the average initial dose was 3.1 grams.<sup>39</sup> In one study, a medium oral dose of dried *Psilocybe Mexicana* was considered to be 2 grams.

For synthetic psilocybin, higher doses of psilocybin (20–30 mg/70 kg) directly correlate to positive persisting effects on behaviour, attitude, mood, and general outlook on life up to 14 months after follow-up, and an oral dose of 25 mg psilocybin (correlating to roughly 0.3 mg/kg of body weight) is considered to be within the therapeutic window.<sup>28</sup>

#### Can I overdose on psilocybin?

Psilocybin overdose is very rare. One such report of psilocybin overdose and subsequent fatality was specifically due to cardiac arrest, 2–3 h after psilocybin ingestion, in a 24-year-old female who, 10 years prior, had a heart transplant due to end-stage rheumatic heart disease.<sup>28</sup>

#### Physiologic effects of psilocybin

Psilocybin produces an altered state of consciousness including changes in perception, mood, and thought process. The most commonly reported experiences are visual and auditory hallucinations, synesthesia, heightened emotions, and a sense of spiritual insight or connectedness.<sup>6</sup> The duration and intensity of effects are subject to individual variations as well as dosage, mindset, and setting.

Psilocybin can cause physical effects that typically last for a few hours. These can include dilated pupils, increased heart rate and blood pressure, dry mouth, loss of appetite, nausea, and muscle weakness. It is essential to note that these effects are usually mild and short-lived.

Despite its low toxicity and potential for addiction, the consumption of psilocybin can come with side effects that will be discussed in a later section.

### Duration of effect

The duration of psilocybin's effects can vary greatly depending on various factors, such as the dosage, individual metabolism, and the setting in which it is consumed. In general, the effects of psilocybin can range from 4-6 hours.<sup>27</sup> However, anecdotal evidence suggests that the effects can last much longer,

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with some users reporting lingering feelings and changes in perception for days or even weeks after consumption.<sup>39</sup>

It is important to note that the duration of psilocybin's effects also depends on the type of mushroom. Some varieties may have a shorter duration, while others may provide a more prolonged experience. In addition, individual tolerance and sensitivity play a significant role in how long the effects will last.

#### Effects

Common effects of psilocybin can include:

- Compromised motor functions
- Disorientation
- Dizziness
- Ego death
- Extreme difficulty with cognitive tasks
- Life-changing introspective or philosophical insights
- Mystical experience and intense feelings of wonder
- Nausea
- Strong fear and anxiety (extreme "bad trip" experiences)
- Synesthesia
- Time becoming meaningless
- Very strong open- and closed-eye visions (e.g., memories coming to life)

# Safety Considerations when Using Psilocybin

### Absolute contraindications

Although psilocybin has shown promising results in treating mental health conditions such as depression and PTSD, there are certain contraindications to consider. Contraindications refer to situations where the use of a particular medication or substance should not be used due to the risk of harm to an individual. It is crucial to consider the contraindications and consult with a healthcare professional before using this substance.

While considered to be generally safe,<sup>40</sup> there are a few factors to take into consideration before using psilocybin. First, we do not have sufficient evidence yet to indicate that psilocybin is safe for individuals with a history of psychosis or

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schizophrenia.<sup>41</sup> Additionally, those with a family history of these disorders may also want to avoid using psilocybin as a precautionary measure.<sup>42</sup>

Another important contraindication for psilocybin use is any existing heart conditions or high blood pressure. Psilocybin can increase heart rate and blood pressure which can be dangerous for individuals with pre-existing cardiovascular issues, though these effects are generally short-lived and resolve after the effect of the psychedelic has subsided. For example, psilocybin was found to only moderately elevate blood pressure sixty minutes following ingestion.<sup>70</sup> Administration of psilocybin likely provides no cause for concern in healthy subjects, but subjects suffering from cardiovascular conditions, such as untreated hypertension, should take caution using psilocybin. It is important to consult with a healthcare professional before using psilocybin if an individual has any heart-related concerns.

Pregnant or breastfeeding women should also avoid using psilocybin as there is limited research on the effects of this substance on developing fetuses and infants.<sup>42</sup> It is always best to err on the side of caution when it comes to using substances during pregnancy and breastfeeding.

Finally, it is important to note that while psilocybin has shown potential in treating substance use disorders, it should only be used by those seeking to treat those disorders under proper supervision and guidance from a healthcare professional.

#### Relative contraindications/warnings

One of the most important aspects to keep in mind are the relative contraindications for psilocybin use. Relative contraindications refer to factors that may increase the risk of adverse effects or complications when using a drug. These factors can vary from individual to individual and may include pre-existing medical conditions, medications being taken, and previous experiences with psychedelics.<sup>43</sup>

According to studies, common relative contraindications for psilocybin use include cardiovascular diseases, epilepsy, and psychotic disorders.<sup>42</sup> These conditions may increase the risk of adverse effects such as increased heart rate, seizures, or exacerbation of psychotic symptoms when using psilocybin. It is recommended that individuals with these conditions consult with their healthcare provider before considering psilocybin therapy.

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Also, certain medications may interact with psilocybin and can result in adverse reactions. These include antidepressants, antipsychotics, and MAO inhibitors.<sup>42</sup> It is essential for anyone taking prescription medications to consult with their healthcare providers before starting psilocybin therapy. In some cases, it may be necessary to temporarily discontinue these medications before the psilocybin session.

In addition, previous negative experiences with psychedelics may also be considered a relative contraindication.<sup>42</sup> This is especially relevant for individuals who have a history of trauma or those with severe anxiety or depression.

It is important to note that these relative contraindications do not necessarily mean that psilocybin cannot be used in these cases. However, it highlights the need for careful screening by a healthcare provider before use and close monitoring during therapy sessions.

#### Challenging experiences

Challenging experiences are not an uncommon occurrence when using psychedelics. They may be related to the following, but they also sometimes just happen, even if the user has taken all the proper precautions. It is best to be aware that they are a possibility and that having the proper support system is crucial should you have a challenging experience.

- Dosage: The amount of psilocybin consumed can greatly impact the intensity and duration of its effects. Higher doses can increase the likelihood of challenging experiences.<sup>41</sup>
- Set and Setting: The mindset and environment in which psilocybin is consumed can also play a significant role in how someone responds to it. If an individual is feeling anxious or in an unfamiliar or unsafe setting, this may increase the risk of challenging experiences.<sup>44</sup>
- Underlying Mental Health Conditions: Psilocybin has been shown to have potential therapeutic benefits for certain mental health conditions, but it can also exacerbate symptoms for those with underlying mental health issues such as schizophrenia or bipolar disorder.<sup>41</sup> It is important to consult with a healthcare professional before using psilocybin if you have any pre-existing mental health conditions.
- Interaction with Other Substances: Mixing psilocybin with other substances, such as alcohol or prescription medications, can lead to challenging experiences.<sup>41</sup> It is important to research potential

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interactions and avoid mixing substances without proper knowledge and guidance.

#### **Responding to challenging experiences**

- Changing the Environment: If someone is feeling overwhelmed or anxious, changing the setting to a more comfortable and safer environment can help alleviate some of the negative effects.
- Practicing Mindfulness: Focusing on breathing and grounding techniques can help individuals stay present and manage any discomfort they may be experiencing.
- Seeking Support: If someone is struggling with negative interactions, it is important to have a supportive and understanding individual nearby who can provide reassurance and assistance if needed. The Fireside Project offers free, confidential, non-clinical emotional support by phone and text message to people in the midst of psychedelic experiences, people exploring the meaning of past psychedelic experiences, and people who are supporting others during psychedelic experiences. Individuals can call or text 62-FIRESIDE for support and guidance.
- In the Canadian Psychedelic Survey (CPS), which is a survey to gather real-world evidence about psychedelic drug use in Canada, In the survey, over half (56%) of those who had an intense challenging experience reported that "some good" came from the experience after-the-fact.<sup>72</sup> Although challenging experiences are not uncommon, these experiences may provide a means for selfexploration, general mental well-being, and personal growth.

### Interactions with other drugs

Data regarding psilocybin's interaction with other drugs is relatively limited.

- **Cannabis**: Cannabis has the potential to enhance the psychedelic nature of the mushrooms.<sup>45</sup>
- Alcohol: Abstain from alcohol while consuming psilocybin.<sup>46</sup>
- Adderall and other stimulants, Xanax, and other benzodiazepines: These are powerful psychoactive drugs and psychedelic use should be approached with extreme caution by individuals who regularly take any of these substances.

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• **Antidepressants**: While there is still limited empirical evidence available on the interactions between common serotonin reuptake inhibitors (SSRIs) and psilocybin, there is some evidence to suggest that chronic administration of serotonergic antidepressants reduces the subjective effects of classic psychedelics, such as LSD and psilocybin. In a summary of results from online surveys and online interviews, Bonson noted that individuals taking serotonin-selective antidepressants had a decrease or abolishment of their response to psychedelics.<sup>47</sup> In another study examining the effect of buspirone, a common anxiolytic (anti-anxiety) medication acting as a serotonin receptor agonist, buspirone reduced psilocybin-induced visual perceptual changes.<sup>48</sup> Anecdotal user reports from Erowid, a non-profit educational organization that provides information about psychoactive plants and chemicals, frequently report a reduction or absence of effects of psychedelics while using common SSRIs.<sup>49</sup>

#### Other drug risks

• One of the primary concerns in combining psychedelics with psychiatric medications is the risk of serotonin toxicity or serotonin syndrome, a rare but potentially life-threatening condition precipitated by the use of serotonergic drugs.<sup>50</sup> Current evidence-based research suggests that the likelihood of toxicity in interactions between SSRIs and psilocybin is low.<sup>51</sup>

• More recently, in a study on the effects of psilocybin, individuals using escitalopram (i.e., Lexapro), a common selective SSRI, showed no relevant effects on the positive mood effects of psilocybin, but escitalopram significantly reduced negative effects of psilocybin, including anxiety and adverse cardiovascular effects.<sup>52</sup> For the study, participants either received 10mg of escitalopram daily for seven days followed by 20mg daily for the next seven days, including the day of psilocybin administration, or 14 days of placebo pre-treatment before psilocybin administration. The researchers found that pre-treatment with escitalopram did not alter the pharmacokinetics of psilocin — the active compound that the prodrug psilocybin is converted into in humans by the process of dephosphorylation. These results suggest that escitalopram and psilocybin can be safely administered together.

#### Side effects/adverse events

While psilocybin is generally safe, it is important to be aware of its potential side effects and adverse events. Research has shown that the severity and frequency of psilocybin side effects may be dose-dependent. For example, Perez and colleagues<sup>53</sup> found significant dose-response associations for various side effects, including physical discomfort, blood pressure increase,

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nausea/vomiting, headache/migraine, and the risk of prolonged psychosis. The most common adverse events were transient, mild to moderate headache and nausea, and a significant dose association was observed with a mostly ascending curve, suggesting that the highest doses are most likely to generate the most side effects. This means that the higher the dosage of psilocybin, the more likely it is to experience adverse reactions and the stronger those reactions may be. In controlled conditions, psychological discomfort during psychedelic trips can occur at higher doses, but panic reactions are easily managed with psychological support.

To minimize the risk of side effects and adverse events, it is crucial to use psilocybin in a safe and controlled environment. This includes having a trusted and experienced guide or therapist present during the session. It is also essential to consult with a healthcare professional before using psilocybin, especially if you have any underlying medical conditions or are taking any medications.

Notably, in Unlimited Sciences' large-scale naturalistic psilocybin study,<sup>9</sup> only six respondents (0.4%) reported seeking medical care, and 52 (3.4%) reported seeking psychological care during or in the 1–3 days after the experience. These ranged from mild (e.g., "headache pill, aspirin") to more severe adverse events, e.g., "I ended up fainting because I lost my self-identity and panicked. I did not know who anyone was or who I was." Another participant wrote, "I went to the ER for suicidal ideation." Most incidents of seeking psychological support described calling a friend or family member, or speaking to a counselor or therapist after the experience for integration purposes and did not represent acute adverse events. Regarding persisting negative effects, 7–11% of participants reported persisting negative effects across follow-up time points. The most commonly reported persisting negative effects after psilocybin use were mood fluctuations (n = 55; 4.7% at 2–4 weeks, and n = 20; 3.0% at 2–3 months) and depressive notions (n = 37; 3.1% at 2–4 weeks, and n = 11; 1.7% at 2–3 months).

#### Side effects associated with psilocybin include:

- Nausea and stomach discomfort are common side effects reported by individuals who have used psilocybin. This can be attributed to the way psilocybin interacts with serotonin receptors in the gut.
- Headaches and muscle tension have also been reported as mild negative side effects of psilocybin. Drinking plenty of water and staying hydrated may help alleviate these symptoms.

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- In some cases, psilocybin can trigger feelings of anxiety and paranoia.
- Psilocybin is known for its ability to alter perception and mood, which can also lead to feelings of confusion or disorientation. These effects are typically short-lived and wear off as the drug metabolizes in the body.
- Increased heart rate and blood pressure. These physical effects can be particularly dangerous for individuals with pre-existing heart conditions.
- Anxiety, paranoia, panic attacks, and dissociative episodes. Research has shown that individuals who consume high doses of psilocybin are at a higher risk of developing these negative mental states.<sup>54</sup> In addition, individuals may experience flashbacks or persistent visual disturbances long after the initial use of psilocybin. These symptoms can significantly impact an individual's daily life and may require professional help to manage.
- Hallucinogen Persisting Perception Disorder (HPPD) is a disorder characterized by the persistence of perceptual disturbances, mainly visual, that occur after the use of hallucinogenic drugs.<sup>55</sup> These disturbances are similar to those experienced during intoxication but happen in the absence of drug use. HPPD can be a distressing and debilitating condition for those who suffer from it. The most common symptoms of HPPD are visual disturbances, including seeing halos or auras around objects, seeing trails or movement in stationary objects, and experiencing changes in color perception.<sup>55</sup> However, some individuals may also experience other sensory disturbances such as auditory hallucinations or tactile sensations.<sup>56</sup> To be diagnosed with HPPD, an individual must have experienced one or more of these symptoms for at least a month after stopping the use of hallucinogenic drugs. It is also essential to rule out other underlying medical or psychiatric conditions that may cause similar symptoms. The exact mechanism behind HPPD is still not fully understood. However, research suggests that it may involve changes in brain chemistry and neural pathways due to the use of hallucinogenic drugs.<sup>55</sup> Additionally, genetic and environmental factors may also play a role in the development of HPPD. Currently, there is no specific treatment for HPPD. However, some medications used for other psychiatric disorders such as antidepressants or anti-anxiety drugs may help alleviate symptoms in some individuals.<sup>55</sup>

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# What is the Current Legal Status of Psilocybin?

#### North America

The Current State of Legalization and Decriminalization of Psychedelics in the United States as of August 2023 can be read in detail in our Unlimited Sciences blog, which described state-by-state updates.

In the United States, psilocybin is classified as a Schedule I drug under the Controlled Substances Act. This classification is intended for drugs with no medical use which have a high potential for abuse. In 2018, Denver, Colorado became the first city in the United States to decriminalize the possession and use of psilocybin mushrooms. Since then, several other cities such as Oakland, California, and Ann Arbor, Michigan have also decriminalized psilocybin. Oregon was the first state in the United States to decriminalize psilocybin and legalize adult use of psilocybin at licensed centers.

Psilocybin is illegal in Canada and is strictly prohibited under Schedule III of the Controlled Drugs and Substances Act (CDSA). The federal government's move to decriminalize personal possession of certain controlled substances in British Columbia in 2023 did not impact the legal status of psilocybin in the province. Although psilocybin is openly sold online and even in storefronts in some Canadian cities, possession, trafficking, cultivation, import, and export of psilocybin and psilocin remains 100% illegal everywhere in Canada, unless one has received an applicable license or exemption.

In 2020, Health Canada began granting select individuals legal access to psilocybin for therapeutic purposes by means of Section 56 exemptions under the Controlled Drugs and Substances Act. This marked the first time that non-study participants in Canada garnered legal access to psilocybin since the substance's criminalization in the 1970s. In January 2022, Health Canada amended regulations pertaining to the Special Access Program (SAP). The new regulations allow medical professionals to request psilocybin for patients with serious or life-threatening conditions where other therapies fail to help a patient or are otherwise unsuitable or unavailable in Canada.

### Europe

In most European countries, psilocybin is illegal for recreational use. However, some countries have more relaxed laws towards its use and possession, including the Netherlands, Czech Republic, Spain, and Portugal. For example,

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psilocybin truffles -masses of mycelium containing the fruiting body - are legal in the Netherlands, but not the mushrooms themselves.

#### South America

Uruguay, Argentina, Colombia, Peru, and Bolivia have decriminalized or legalized possession of small amounts of all drugs for personal use.

#### Asia

Psilocybin use and possession are mostly illegal in Asian countries.

# **Psychedelic-Assisted Therapy**

Psychedelic-assisted therapy is a form of mental health treatment that utilizes psychedelic substances, such as psilocybin, to facilitate therapeutic experiences and promote emotional healing.<sup>57</sup> This type of therapy often involves multiple sessions with a therapist and can include talk therapy before and after the psychedelic experience.

Psychedelic-assisted therapists should have both a certification in a medical or therapy field and who also has done extensive training in psychedelic-assisted therapy.<sup>58</sup> (Note that in Oregon, facilitators need only to have graduated from a facilitator training program licensed by the state of Oregon.)

Psychedelic-assisted therapists need to do proper screening procedures to assess for any potential risks or contraindications, as well as provide a safe and supportive environment during sessions.<sup>59</sup> Practitioners must also adhere to ethical guidelines and principles, such as confidentiality and informed consent.

#### Cost

The exact cost of psilocybin-assisted therapy may vary depending on various factors, such as the location and specific treatment protocol. For example, the first licensed facility where people can legally buy and consume psilocybin in the U.S. will charge over \$2, 800 - \$3,500 depending on the dosage.<sup>60</sup> In the United Kingdom, The expected healthcare cost of psychedelic-assisted therapy varied from £6132 to £7652 depending on the price of psilocybin.<sup>61</sup> Most psychedelic retreats start around \$3,500 - \$6,000, but prices can reach up to \$10,000.<sup>62</sup>

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However, more affordable retreats may cost as low as \$675 to \$2995 per person.<sup>63</sup> The cost of psilocybin therapy is not limited to just the treatment session itself. It also typically includes pre- and post-treatment consultations, as well as integration therapy to help patients process their experiences and incorporate them into their daily lives.

# How to access psychedelic therapy legally

### **Research Local Laws and Regulations**

Before starting any form of psychedelic therapy, it is essential to research and understand the laws and regulations in the local area. While psilocybin may be legal in some countries or states for medical or religious purposes, it may still be classified as a Schedule I drug in others, meaning it is completely illegal to possess or use. It is also important to note that even if psilocybin is legal in an area, it may still require a prescription or be restricted to certain medical conditions or licensed centers.

### Participate in Clinical Trials

Another way to access psychedelic therapy legally is through participating in clinical trials. As more research is conducted on the potential therapeutic benefits of psilocybin, there are increasing opportunities for individuals to participate in legal and regulated trials. Clinical trials allow for a structured and supervised therapeutic experience, while also contributing to the advancement of scientific knowledge.

### **Retreats in Legal Countries**

Clients who have financial resources may ask a clinician's opinion about traveling to other countries where psychedelic retreats are legal. Indeed, psychedelic tourism is expanding rapidly in countries throughout the world. While this option may circumvent legal restrictions, traveling to international retreat centers carries unique risks. First, organizations that offer retreats may not comply with professional standards that exist in a client's country of origin. Second, some retreat centers may have negligible procedures for screening or preparing participants and therefore may include individuals who are not adequately prepared or stable enough for psychedelic experiences. For these reasons, it is recommended that clients considering traveling to other countries familiarize themselves with guidelines for reducing such risks, such as traveling with trusted companions, conducting thorough research, and understanding norms for psychedelic ceremonies.<sup>64</sup>

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# How to identify quality psilocybin sources

## **Understanding Psilocybin Sources**

Psilocybin can be found in various forms, such as whole mushrooms, dried mushrooms, or extracted powder. It is important to note that not all psilocybin-containing mushrooms are created equal.<sup>4</sup> Some species may contain other harmful compounds that can have adverse effects on the body. Therefore, it is crucial to identify quality sources of psilocybin to avoid any potential risks.

## Cultivation and Harvesting Methods

One of the essential factors in identifying quality psilocybin sources is understanding how the mushrooms are cultivated and harvested. Ideally, psilocybin-containing mushrooms should be grown in a controlled environment using proper techniques. This ensures the purity and potency of the mushrooms. Wild-picked mushrooms can be contaminated with other substances or mold, making them unsafe for human consumption.<sup>4</sup>

### Appearance and Smell

Quality psilocybin mushrooms should have a distinct appearance and smell and the caps of the mushroom should be dark in color and have spores that are evenly spread underneath.<sup>4</sup> Psilocybin mushrooms should also have a noticeable mushroom smell and not have any off-putting odors. Mushrooms that appear slimy, discolored, or have a pungent odor may indicate that they are either old or contaminated.

# **Testing and Lab Analysis**

To ensure the quality and purity of psilocybin sources, some individuals choose to send their mushrooms for lab analysis. This process can provide a breakdown of the psilocybin and other compounds present in the mushrooms. It can also detect any potential contaminants, providing peace of mind before consumption.

# Safety Precautions

It is vital to take necessary safety precautions when consuming psilocybin, regardless of its source. For first-time users, it is recommended that psilocybin should be taken with a facilitator present after consultation with a healthcare provider for the safety of those consuming and of others.<sup>11</sup> For more experienced users, however, our recent investigation of naturalistic psilocybin use, which is use outside of a clinical setting, showed that participants reported primarily using psilocybin alone (n = 667;

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43.0%) and at home (n = 1,081; 69.7%) and the presence of a sitter/guide was not a significant predictor of health outcomes.<sup>39</sup>

# Preparation of psilocybin

One of the most common methods of preparing psilocybin is by drying the mushrooms containing it.<sup>10</sup> This involves simply picking fresh mushrooms, removing their stems, and placing them in a well-ventilated area until they are completely dry. Once dried, the mushrooms can be consumed as they are or ground into a fine powder for easier ingestion.

Another popular method is the extraction of psilocybin from the mushrooms. This involves using solvents, such as alcohol or water, to extract the compound from the mushroom material.<sup>65</sup> The resulting solution can then be evaporated to leave a concentrated form of psilocybin, which can be further processed into capsules or incorporated into food or beverages. This method allows for precise dosing and eliminates any potential gastrointestinal discomfort that may occur with consuming whole mushrooms.

With the increasing research interest in recent years, there has also been a rise in the production of synthetic psilocybin.<sup>66</sup> This involves using chemical reactions to create the compound in a laboratory setting. Synthetic psilocybin is often used in clinical research as it provides a consistent and controlled form of the compound for study purposes.<sup>66</sup> Synthetic drugs are manufactured with high purity and a defined concentration of active ingredient(s).<sup>67</sup> Natural products may also contain a multiplicity of compounds/secondary metabolites that may not be of particular interest and may even be harmful.

Perhaps one of the most innovative methods of preparing psilocybin is through biosynthesis. This involves using genetically modified bacteria or fungi to produce psilocybin in a controlled environment.<sup>68</sup>

# What to expect from a psilocybin experience

A psilocybin experience is an altered state of consciousness that can occur after ingesting psilocybin or magic mushrooms. It is often described as a profound and mystical experience that can have long-lasting effects on one's perception, emotions, and thoughts.<sup>69</sup> The intensity and duration of the experience can vary depending on factors such as dosage, set (mindset before taking the substance), setting (physical environment where it takes place), and individual sensitivity.<sup>69</sup>

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However, prior to any experience, it is important to note that preparation is key. This includes not only physical preparation, such as ensuring a safe and comfortable setting but also mental and emotional preparation.<sup>69</sup> It is important to approach a psilocybin experience with an open and positive mindset, as well as a willingness to confront any challenging emotions or thoughts that may arise. Depending on the dose, it is also recommended to have a trusted and experienced trip sitter present.<sup>69</sup>

### The onset and peak of the experience

After ingesting psilocybin, it typically takes between 20 minutes to an hour for an individual to feel the effects.<sup>26</sup> During this time, individuals may experience changes in perception, such as heightened senses or visual distortions. These effects will continue to intensify until reaching a peak, which can last anywhere from 2-6 hours depending on dosage and individual factors.<sup>26</sup> It is important to remember that every psilocybin experience is unique and can vary greatly in intensity.

### The intense experience

As the psilocybin experience reaches its peak, individuals may experience intense changes in perception and thought patterns. This can include feelings of euphoria, introspection, and a sense of interconnectedness with the world around them.<sup>69</sup> It is also common to experience a dissolution of the ego, or a sense of losing oneself.<sup>69</sup> This sensation can be both exhilarating and frightening for some individuals. It is important to remember that these sensations are temporary and will subside as the effects wear off.

### Comedown

The comedown of a psilocybin experience can last for several hours after the peak and includes a gradual return to baseline mental state. Users may feel euphoric, fatigued, emotionally drained, and/or introspective during this stage.<sup>70</sup>

### Navigating challenging experiences

While many individuals have positive and transformative experiences with psilocybin, it is also important to acknowledge that challenging experiences can occur. Challenges may include feelings of anxiety, fear, or confronting difficult emotions or past traumas.<sup>44</sup> It is important to have a support system in place before embarking on a psilocybin experience, as well as the ability to communicate with

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your trip sitter if necessary.<sup>71</sup> However, although unpleasant, these challenges often lead to growth and healing in the long term. In the Canadian Psychedelic Survey (CPS), which is a survey to gather real-world evidence about psychedelic drug use in Canada, In the survey, over half (56%) of those who had an intense challenging experience reported that "some good" came from the experience after-the-fact.<sup>72</sup> Although challenging experiences are not uncommon, these experiences may provide a means for self-exploration, general mental well-being, and personal growth.

# **Components of Psilocybin Therapy**

#### Preparation

Psilocybin journeys can be intense and overwhelming experiences. Without proper preparation, individuals may feel anxious, confused, or even have a challenging trip. Therefore, preparation is an essential step towards having a safe, transformative experience with psilocybin.<sup>69</sup>

One crucial aspect of preparation is educating oneself about psilocybin. It is essential to consult reliable sources, as education not only provides a better understanding of what to expect but also helps in setting realistic expectations for the journey.<sup>69</sup>

Further, seek guidance from psychedelic integration therapists or trusted professionals who can prepare you for a psilocybin experience by providing valuable insights, tips, and tools for navigating the journey.

In addition to preparing oneself mentally and physically, it is equally essential to prepare emotionally for a psilocybin journey. As psilocybin can bring up intense emotions and experiences, it is vital to be in a stable emotional state before embarking on the journey.<sup>69</sup> This could involve practicing mindfulness and self-care activities leading up to the journey, as well as addressing any underlying emotional issues.

It is also crucial to have a support system in place during and after the psilocybin journey. Support systems can include a trusted friend or therapist who can provide guidance and comfort during challenging moments.<sup>73</sup> It is normal to experience a range of emotions during and after the journey, so having someone to talk to can be immensely helpful.

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It is also essential to follow safety precautions when preparing for a psilocybin journey. This includes knowing the correct dosage, being aware of potential drug interactions, and having a facilitator, therapist, or trip-sitter present during the experience.<sup>69</sup> It is also recommended to have emergency contact information readily available in case of any unforeseen circumstances.

#### Set and Setting

As more research is conducted, it is becoming clear that the effects of psilocybin are highly dependent on two key factors: set and setting.

#### What is Set?

Set refers to an individual's mindset or mental state before embarking on a psilocybin journey. This includes their expectations, beliefs, emotions, and overall psychological state. Research has shown that those who approach a psilocybin experience with intention and respect are more likely to have positive outcomes.<sup>69</sup> This is because set can greatly influence the subjective effects of psilocybin, including emotions, thought patterns, and overall experience.<sup>74</sup>

#### What is Setting?

Setting refers to the physical and social environment in which a psilocybin journey takes place. This includes factors such as lighting, music, comfort level, and support from trusted individuals.<sup>69</sup>

#### Why Set and Setting are Important

Research has shown that the effects of psilocybin can vary significantly depending on an individual's set and setting. Studies have found that psilocybin-induced mystical experiences were enhanced when individuals had a positive mindset and were in a supportive, safe environment.<sup>38</sup> On the other hand, negative emotions and an uncomfortable setting increased the likelihood of having unpleasant or even challenging experiences.<sup>71</sup>

#### **Recommendations for Set and Setting**

Some recommendations include doing something like breathwork or meditation to prepare one's mindset prior to the experience,

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approaching the experience with intention, being in a comfortable and familiar environment, having support from trusted individuals, and choosing appropriate music or other stimuli.<sup>76</sup> It is also recommended to have a guide or sitter present during the experience who can provide reassurance and support.<sup>69</sup>

#### Integration

Integration refers to the process of incorporating insights gained during a psychedelic experience into one's daily life.<sup>75</sup> This includes reflecting on insights gained during the journey and applying them to personal growth and well-being. Integration can also involve addressing any challenging emotions or experiences that may have arisen during the journey. This is crucial as the insights gained during a psilocybin journey can be profound and transformative, but without integration, they may not have lasting effects.<sup>76</sup>

A psilocybin journey can be a deeply transformative experience, often bringing about profound insights and shifts in perspective. However, without proper integration, these realizations may fade away over time or even become overwhelming. The goal of integration is to make lasting changes based on the insights gained from a psilocybin journey.

#### How to integrate after a psilocybin journey

Some commonly recommended integration activities include:<sup>11,69,77</sup>

- Finding an experienced guide or therapist: Having a trained professional to provide guidance and support during your psilocybin journey can greatly enhance the integration process.
- 2. Journaling: Writing down thoughts and emotions can help individuals process their experiences and gain deeper insights.
- 2. Therapy or Counseling: Working with a licensed mental health professional who is familiar with psilocybin therapy can aid in the integration process.
- 3. Mindfulness Practices: Engaging in mindful activities such as meditation, yoga, or nature walks can help individuals stay present and connected to themselves.
- Support Groups: Connecting with others who have had similar experiences can provide a sense of community and support during the integration process.

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 Practicing self-care: A psilocybin journey can be physically, mentally, and emotionally demanding. After the experience, it is important to prioritize self-care activities such as rest, healthy eating, exercise, and relaxation techniques.

# Debunking the Myths Surrounding Psilocybin

Some of the most common myths surrounding psilocybin and psychedelics are:

- Myth #1: Psychedelics are dangerous and can cause permanent damage This belief stems from the stigma surrounding illegal drugs and their perceived harmfulness. However, numerous scientific studies have shown that psychedelics, when used responsibly and in a controlled setting, are not toxic or addictive. On the contrary, they have been found to have therapeutic benefits for certain conditions, including helping individuals overcome addictions, rather than causing them.
- Myth #2: Psychedelics are just for recreational use and have no real medical value There is a growing body of research showing their potential therapeutic benefits. Clinical trials have shown promising results in using psilocybin to treat a number of conditions, including depression, end-of-life anxiety, and addiction.
- Myth #3: All psychedelics have the same effects Different types of psychedelics produce distinct experiences and may have different therapeutic potential.
- Myth #4: Psychedelics are only used by young people

While it is true that there is a higher prevalence of psychedelic use among younger individuals, research has shown that they can also be beneficial for older adults. Older age is associated with many health conditions that could potentially benefit from psychedelic-assisted therapy, including the distress associated with a serious illness, depression, PTSD, prolonged grief disorder, substance use disorders, and dementia. Studies in healthy older adults suggest that psychedelics are safe when used in an optimal, controlled setting.<sup>78</sup> However, published research on psychedelic medications has suggested that they are relatively safe when given in controlled conditions, few older people with multimorbidity have been included in clinical trials to date, making the generalizability to older adults with multimorbidity uncertain.<sup>78</sup>

*Myth #5: Psychedelics are a gateway to more lethal drugs* Singh, Gaughen, Hill, Morski, & Lowe. Psilocybin Guide. Page 33 of 38

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There is no evidence to support this claim. Research has shown that psychedelics can have the opposite effect, that is helping individuals overcome addiction and reducing substance use. The therapeutic potential of psychedelics may actually reduce the risk of developing substance use disorders.

https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(16)30065-7/fulltext.

Singh, Gaughen, Hill, Morski, & Lowe. Psilocybin Guide. Page  $34~{\rm of}~38$ 

<sup>&</sup>lt;sup>1</sup> Rucker, J.J.H., J. Iliff, and D.J. Nutt, *Psychiatry & the psychedelic drugs. Past, present & future.* Neuropharmacology, 2018. 142: p. 200-218. Available from: <u>https://www.ncbi.nlm.nih.gov/pubmed/29284138</u>.

<sup>&</sup>lt;sup>2</sup> Guzmán, G., J. Allen, and J. Gartz, *A Worldwide geographical distribution of the Neurotropic Fungi, an analysis and discussion.* Ann Mus Civ Rovereto, 1998. 14. Available from:

https://www.researchgate.net/publication/237398624 A Worldwide geographical distribution of the Neurotro pic Fungi an analysis and discussion#fullTextFileContent.

<sup>&</sup>lt;sup>3</sup> HOFMANN, A., HEIM, R., BRACK, A., & KOBEL, H. (1958). Psilocybin, ein psychotroper Wirkstoff aus dem mexikanischen Rauschpilz Psilocybe mexicana Heim [Psilocybin, a psychotropic substance from the Mexican mushroom Psilicybe mexicana Heim]. Experientia, 14(3), 107–109. <u>https://doi.org/10.1007/BF02159243</u>

<sup>&</sup>lt;sup>4</sup> Stamets, P., *Psilocybin mushrooms of the world: an identification guide*. 2023, Berkley, CA: Ten Speed Press. Available from:

https://books.google.com/books?hl=en&lr=&id=DISeEAAAQBAJ&oi=fnd&pg=PR9&dq=Psilocybin+mushrooms+of+t he+world:+an+identification+guide&ots=oVG-

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<sup>&</sup>lt;sup>5</sup> Carhart-Harris, R.L., et al., *Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study.* Lancet Psychiatry, 2016. 3(7): p. 619-27. Available from:

<sup>&</sup>lt;sup>6</sup> Ross, S., et al., *Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial.* J Psychopharmacol, 2016. 30(12): p. 1165-1180. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5367551/</u>.

<sup>&</sup>lt;sup>7</sup> Bogenschutz, M.P., et al., *Psilocybin-assisted treatment for alcohol dependence: a proof-of-concept study*. J Psychopharmacol, 2015. 29(3): p. 289-99. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25586396.

<sup>&</sup>lt;sup>8</sup> Khan, A.J., et al., *Psilocybin for Trauma-Related Disorders*. Curr Top Behav Neurosci, 2022. 56: p. 319-332. Available from: <u>https://link.springer.com/chapter/10.1007/7854\_2022\_366</u>.

<sup>&</sup>lt;sup>9</sup> Carod-Artal F. J. (2015). Hallucinogenic drugs in pre-Columbian Mesoamerican cultures. Neurologia (Barcelona, Spain), 30(1), 42–49. <u>https://doi.org/10.1016/j.nrl.2011.07.003</u>

<sup>&</sup>lt;sup>10</sup> Ross, S., S. Franco, and C. Reiff, Agin-Liebes, Gabrielle, *Psilocybin*, in *Handbook of Medical Hallucinogens*, C. Grob, S. and J. Grigsby, Editors. 2022, The Guilford Press: New York, NY. p. 181-214. Available from: <u>https://www.google.com/books/edition/Handbook of Medical Hallucinogens/ebb2DwAAQBAJ?hl=en&gbpv=1&</u>

dq=Handbook+of+Medical+Hallucinogens&printsec=frontcover.

<sup>&</sup>lt;sup>11</sup> Strassman, R.J., *The psychedelic handbook*. 2022, Berkley, CA: Ulysses Press. Available from: <u>https://www.rickstrassman.com/publications/the-psychedelic-handbook/</u>.

<sup>&</sup>lt;sup>12</sup> Fischer, R., *A cartography of the ecstatic and meditative states*. Science, 1971. 174(4012): p. 897-904. Available from: <u>https://www.science.org/doi/10.1126/science.174.4012.897?url\_ver=Z39.88-</u>2003&rfr\_id=ori:rid:crossref.org&rfr\_dat=cr\_pub%20%200pubmed.

<sup>&</sup>lt;sup>13</sup> Labate, B.C. and G.M. Pacheco, *The historical origins of Santo Daime: Academics, adepts, and ideology.*, in *The internationalization of ayahuasca*, B.C. Labate and H. Jungaberle, Editors. 2011, LIT Verlag Münster: Germany. p. 71-84. Available from: <u>https://books.google.com/books?hl=en&lr=&id=49i8-</u>

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<u>CzmY\_oC&oi=fnd&pg=PA21&dq=The+internationalization+of+ayahuasca&ots=6acJ971fUQ&sig=UphdQevBy9lQND</u> wUjlZ2qlugYLQ#v=onepage&q=The%20internationalization%20of%20ayahuasca&f=false.

<sup>14</sup> Belouin, S. J., & Henningfield, J. E. (2018). Psychedelics: Where we are now, why we got here, what we must do. Neuropharmacology, 142, 7–19. <u>https://doi.org/10.1016/j.neuropharm.2018.02.018</u>

<sup>15</sup> Davis, A.K., et al., *Effects of Psilocybin-Assisted Therapy on Major Depressive Disorder: A Randomized Clinical Trial.* JAMA Psychiatry, 2021. 78(5): p. 481-489. Available from:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7643046/.

<sup>16</sup> Gukasyan, N., et al., *Efficacy and safety of psilocybin-assisted treatment for major depressive disorder: Prospective 12-month follow-up.* J Psychopharmacol, 2022. 36(2): p. 151-158. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8864328/</u>.

<sup>17</sup> Goldberg, S.B., et al., *The experimental effects of psilocybin on symptoms of anxiety and depression: A metaanalysis.* Psychiatry Res, 2020. 284: p. 112749. Available from:

https://www.sciencedirect.com/science/article/abs/pii/S016517811930811X?via%3Dihub.

<sup>18</sup> Moreno, F.A., et al., *Safety, tolerability, and efficacy of psilocybin in 9 patients with obsessive-compulsive disorder.* J Clin Psychiatry, 2006. 67(11): p. 1735-40. Available from: <u>https://pubmed.ncbi.nlm.nih.gov/17196053/</u>.

<sup>19</sup> Krediet, E., et al., *Reviewing the Potential of Psychedelics for the Treatment of PTSD.* Int J

Neuropsychopharmacol, 2020. 23(6): p. 385-400. Available from:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7311646/.

<sup>20</sup> Bogenschutz, M.P., et al., *Percentage of Heavy Drinking Days Following Psilocybin-Assisted Psychotherapy vs Placebo in the Treatment of Adult Patients With Alcohol Use Disorder: A Randomized Clinical Trial.* JAMA Psychiatry, 2022. 79(10): p. 953-962. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9403854/</u>.

<sup>21</sup> Johnson, M.W., et al., *Pilot study of the 5-HT2AR agonist psilocybin in the treatment of tobacco addiction*. J Psychopharmacol, 2014. 28(11): p. 983-92. Available from:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4286320/.

<sup>22</sup> Johnson, M.W., A. Garcia-Romeu, and R.R. Griffiths, *Long-term follow-up of psilocybin-facilitated smoking cessation*. Am J Drug Alcohol Abuse, 2017. 43(1): p. 55-60. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5641975/.

<sup>23</sup> Griffiths, R.R., et al., *Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial.* J Psychopharmacol, 2016. 30(12): p. 1181-1197. Available from: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5367557/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5367557/</a>.

<sup>24</sup> Madsen, M.K., et al., *Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels*. Neuropsychopharmacology, 2019. 44(7): p. 1328-1334. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6785028/.

<sup>25</sup> Passie, T., et al., *The pharmacology of psilocybin*. Addict Biol, 2002. 7(4): p. 357-64. Available from: https://www.ncbi.nlm.nih.gov/pubmed/14578010.

<sup>26</sup> Dinis-Oliveira, R.J., *Metabolism of psilocybin and psilocin: clinical and forensic toxicological relevance*. Drug Metab Rev, 2017. 49(1): p. 84-91. Available from:

https://www.tandfonline.com/doi/full/10.1080/03602532.2016.1278228.

<sup>27</sup> Brown, R.T., et al., *Pharmacokinetics of Escalating Doses of Oral Psilocybin in Healthy Adults*. Clin
 Pharmacokinet, 2017. 56(12): p. 1543-1554. Available from: <a href="https://link.springer.com/article/10.1007/s40262-017-0540-6">https://link.springer.com/article/10.1007/s40262-017-0540-6</a>.

<sup>28</sup> Lowe H, Toyang N, Steele B, Valentine H, Grant J, Ali A, Ngwa W, Gordon L. The Therapeutic Potential of Psilocybin. Molecules. 2021 May 15;26(10):2948. doi: 10.3390/molecules26102948. PMID: 34063505; PMCID: PMC8156539.

<sup>29</sup> Studerus, E., et al., Acute, subacute and long-term subjective effects of psilocybin in healthy humans: a pooled analysis of experimental studies. J Psychopharmacol, 2011. 25(11): p. 1434-52. Available from: Sitebs Gauge Markin & Loger Psilopharmacol 38

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<sup>30</sup> Gattuso, J.J., et al., *Default Mode Network Modulation by Psychedelics: A Systematic Review*. Int J Neuropsychopharmacol, 2023. 26(3): p. 155-188. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10032309/.

<sup>31</sup> Roseman, L., et al., *The effects of psilocybin and MDMA on between-network resting state functional connectivity in healthy volunteers.* Front Hum Neurosci, 2014. 8: p. 204. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4034428/.

<sup>32</sup> Ly, C., et al., *Psychedelics Promote Structural and Functional Neural Plasticity*. Cell Rep, 2018. 23(11): p. 3170-3182. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6082376/</u>.

<sup>33</sup> de Vos, C.M.H., N.L. Mason, and K.P.C. Kuypers, *Psychedelics and Neuroplasticity: A Systematic Review Unraveling the Biological Underpinnings of Psychedelics.* Front Psychiatry, 2021. 12: p. 724606. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8461007/</u>.

<sup>34</sup> Strumila, R., et al., *Psilocybin, a Naturally Occurring Indoleamine Compound, Could Be Useful to Prevent Suicidal Behaviors*. Pharmaceuticals (Basel), 2021. 14(12). Available from:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8704767/.

<sup>35</sup> Aronson, J.K., *Meyler's Side Effects of Psychiatric Drugs*. 1st ed. 2008, United States: Elsevier Science. Available from: <u>https://books.google.com/books?id=AmYFTSO8jCkC</u>.

<sup>36</sup> de la Fuente Revenga, M., Jaster, A. M., McGinn, J., Silva, G., Saha, S., & González-Maeso, J. (2022). Tolerance and Cross-Tolerance among Psychedelic and Nonpsychedelic 5-HT2A Receptor Agonists in Mice. ACS chemical neuroscience, 13(16), 2436–2448. Available from: <u>https://doi.org/10.1021/acschemneuro.2c00170</u>

<sup>37</sup> Hutten, N., et al., *Self-Rated Effectiveness of Microdosing With Psychedelics for Mental and Physical Health Problems Among Microdosers.* Front Psychiatry, 2019. 10: p. 672. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6753862/</u>.

<sup>38</sup> Winkelman, M.J., *The Evolved Psychology of Psychedelic Set and Setting: Inferences Regarding the Roles of Shamanism and Entheogenic Ecopsychology*. Front Pharmacol, 2021. 12: p. 619890. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7959790/.

<sup>39</sup> Nayak, S.M., et al., *Naturalistic psilocybin use is associated with persisting improvements in mental health and wellbeing: results from a prospective, longitudinal survey.* Front Psychiatry, 2023. 14: p. 1199642. Available from: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10545967/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10545967/</a>.

<sup>40</sup> Johnson, M.W., et al., *Classic psychedelics: An integrative review of epidemiology, therapeutics, mystical experience, and brain network function.* Pharmacol Ther, 2019. 197: p. 83-102. Available from: <a href="https://www.sciencedirect.com/science/article/abs/pii/S0163725818302158?via%3Dihub">https://www.sciencedirect.com/science/article/abs/pii/S0163725818302158?via%3Dihub</a>.

<sup>41</sup> MacCallum, C.A., et al., *Therapeutic use of psilocybin: Practical considerations for dosing and administration*. Front Psychiatry, 2022. 13: p. 1040217. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9751063/</u>.

<sup>42</sup> Frecska, E., *Therapeutic guidelines: dangers and contra-indications in therapeutic applications of hallucinogens*, in *Psychedelic Medicine*, T. Roberts and M.J. Winkelman, Editors. 2007. p. 69-95. Available from:

https://www.researchgate.net/publication/260515659 Therapeutic guidelines dangers and contraindications in therapeutic applications of hallucinogens#fullTextFileContent.

<sup>43</sup> Johnson, M.W., W. Richards, and R. Griffiths, *Human hallucinogen research: guidelines for safety*. J Psychopharmacol, 2008. 22(6): p. 603-20. Available from:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3056407/.

<sup>44</sup> Bienemann, B., et al., *Self-reported negative outcomes of psilocybin users: A quantitative textual analysis.* PLoS One, 2020. 15(2): p. e0229067. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7034876/</u>.

<sup>45</sup> Kuc, J., et al., *Psychedelic experience dose-dependently modulated by cannabis: results of a prospective online survey.* Psychopharmacology (Berl), 2022. 239(5): p. 1425-1440. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9110465/.

<sup>46</sup> Hillard, J. *Alcohol and hallucinogens*. Alcohol Rehab Guide, 2023. Singhs. Gruther. Hill Marski, & Interscience: Poilogy bioGuide and Straight Children and Straight Child

<sup>47</sup> Bonson, K. R., Buckholtz, J. W., & Murphy, D. L. (1996). Chronic administration of serotonergic antidepressants attenuates the subjective effects of LSD in humans. Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology, 14(6), 425–436. <u>https://doi.org/10.1016/0893-133X(95)00145-4</u>

<sup>48</sup> Sarparast, A., Thomas, K., Malcolm, B. et al. Drug-drug interactions between psychiatric medications and MDMA or psilocybin: a systematic review. Psychopharmacology 239, 1945–1976 (2022). <u>https://doi.org/10.1007/s00213-022-06083-y</u>

<sup>49</sup> <u>https://erowid.org/psychoactives/</u>

<sup>50</sup> Simon LV, Keenaghan M. Serotonin Syndrome. [Updated 2023 Jul 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <u>https://www.ncbi.nlm.nih.gov/books/NBK482377/</u>

<sup>51</sup> Sarparast, A., Thomas, K., Malcolm, B., & Stauffer, C. S. (2022). Drug-drug interactions between psychiatric medications and MDMA or psilocybin: a systematic review. Psychopharmacology, 239(6), 1945–1976. https://doi.org/10.1007/s00213-022-06083-y

<sup>52</sup> Becker, A. M., Holze, F., Grandinetti, T., Klaiber, A., Toedtli, V. E., Kolaczynska, K. E., Duthaler, U., Varghese, N., Eckert, A., Grünblatt, E., & Liechti, M. E. (2022). Acute Effects of Psilocybin After Escitalopram or Placebo Pretreatment in a Randomized, Double-Blind, Placebo-Controlled, Crossover Study in Healthy Subjects. Clinical pharmacology and therapeutics, 111(4), 886–895. <u>https://doi.org/10.1002/cpt.2487</u>

<sup>53</sup> Perez, N., Langlest, F., Mallet, L., De Pieri, M., Sentissi, O., Thorens, G., Seragnoli, F., Zullino, D., Kirschner, M., Kaiser, S., Solmi, M., & Sabé, M. (2023). Psilocybin-assisted therapy for depression: A systematic review and dose-response meta-analysis of human studies. European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology, 76, 61–76. <u>https://doi.org/10.1016/j.euroneuro.2023.07.011</u>

<sup>54</sup> Dos Santos, R.G., et al., *Antidepressive, anxiolytic, and antiaddictive effects of ayahuasca, psilocybin and lysergic acid diethylamide (LSD): a systematic review of clinical trials published in the last 25 years.* Ther Adv Psychopharmacol, 2016. 6(3): p. 193-213. Available from:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4910400/.

<sup>55</sup> Martinotti, G., et al., *Hallucinogen Persisting Perception Disorder: Etiology, Clinical Features, and Therapeutic Perspectives.* Brain Sci, 2018. 8(3). Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5870365/</u>.

<sup>56</sup> Hermle, L., et al., *Hallucinogen-persisting perception disorder*. Ther Adv Psychopharmacol, 2012. 2(5): p. 199-205. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3736944/</u>.

<sup>57</sup> Schenberg, E.E., *Psychedelic-Assisted Psychotherapy: A Paradigm Shift in Psychiatric Research and Development*. Front Pharmacol, 2018. 9: p. 733. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6041963/</u>.

<sup>58</sup> Penn, A. *How to become a psychedelic therapist*. Psychology Today, 2020.

https://www.psychologytoday.com/us/blog/psyche-meets-soul/202011/how-become-psychedelic-therapist.

<sup>59</sup> Pilecki, B., et al., *Ethical and legal issues in psychedelic harm reduction and integration therapy*. Harm Reduct J, 2021. 18(1): p. 40. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8028769/</u>.

<sup>60</sup> Najum, J. *\$3,500: The cost of treatment in America's firts legal psilocybin center*. Microdose, 2023. <u>https://microdose.buzz/news/treatment-in-americas-first-legal-psilocybin-center/</u>.

<sup>61</sup> McCrone, P., Fisher, H., Knight, C., Harding, R., Schlag, A. K., Nutt, D. J., & Neill, J. C. (2023). Cost-effectiveness of psilocybin-assisted therapy for severe depression: exploratory findings from a decision analytic model. Psychological medicine, 53(16), 7619–7626. <u>https://doi.org/10.1017/S0033291723001411</u>

<sup>62</sup> <u>https://psychedelicspotlight.com/these-are-some-of-the-most-affordable-psychedelic-retreats-out-there/</u>

<sup>63</sup> <u>https://psychedelicspotlight.com/oregons-first-licensed-psilocybin-center-charges-2800-for-one-session-are-the-costs-justifiable/</u>

<sup>64</sup> Pilecki, B., Luoma, J.B., Bathje, G.J. et al. Ethical and legal issues in psychedelic harm reduction and integration therapy. Harm Reduct J 18, 40 (2021). <u>https://doi.org/10.1186/s12954-021-00489-1</u>

<sup>65</sup> Cody, J.T., *Chapter 4 Hallucinogens*, in *Handbook of Analytical Separations*, M.J. Bogusz, Editor. 2008, Elsevier Sciences Bry phil 75-201 Available from: Suite: Cal Bry phil 75-201 Availabl

<u>https://www.google.com/books/edition/Forensic\_Science/enpOcRUIZ2gC?hl=en&gbpv=1&dq=Forensic+Science+(</u> Volume+6)+(Handbook+of+Analytical+Separations,+Volume+6)&pg=PR2&printsec=frontcover.

<sup>66</sup> Lea, S. *Synthetic Psilocybin: Cost and Production Methods*. Truffle Report - Psychedelic News, 2021. <u>https://truffle.report/medical-psilocybin-cost-and-production-methods/</u>.

<sup>67</sup> Ali, A., Gifford, ME., Lowe, H., Gordon, L., Grant, J. (2023). Natural vs. Synthetic Psilocybin: The Same or Completely Different?. In: Agrawal, D.C., Dhanasekaran, M. (eds) Mushrooms with Therapeutic Potentials. Springer, Singapore. <u>https://doi.org/10.1007/978-981-19-9550-7\_18</u>

<sup>68</sup> Fricke, J., F. Blei, and D. Hoffmeister, *Enzymatic Synthesis of Psilocybin*. Angew Chem Int Ed Engl, 2017. 56(40): p. 12352-12355. Available from: <u>https://pubmed.ncbi.nlm.nih.gov/28763571/</u>.

<sup>69</sup> Griffiths, R.R., et al., *Psilocybin occasioned mystical-type experiences: immediate and persisting dose-related effects.* Psychopharmacology (Berl), 2011. 218(4): p. 649-65. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3308357/.

<sup>70</sup> Carbonaro, T.M., M.W. Johnson, and R.R. Griffiths, *Subjective features of the psilocybin experience that may account for its self-administration by humans: a double-blind comparison of psilocybin and dextromethorphan.* Psychopharmacology (Berl), 2020. 237(8): p. 2293-2304. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10013695/.

<sup>71</sup> Goldsmith, N., *Things can go wrong: What you need to know*, in *The Psychedelic Explorers Guide*, J. Fadiman, Editor. 2011, Park Street Press: Rochester, TV. Available from:

https://www.google.com/books/edition/The\_Psychedelic\_Explorer\_s\_Guide/\_V0oDwAAQBAJ?hl=en&gbpv=1&dq =The+psychedelic+explorer%27s+guide&printsec=frontcover.

<sup>72</sup> Lake, S., & Lucas, P. (2023). The Canadian Psychedelic Survey: Characteristics, Patterns of Use, and Access in a Large Sample of People Who Use Psychedelic Drugs. Psychedelic Medicine, 1(2), 98-110. https://doi.org/10.1089/psymed.2023.0002

<sup>73</sup> Aixalà, M.B., *Psychedelic integration: Psychotherapy for non-ordinary states of consciousness*. 2022, London: Synergetic Press. Available from:

https://www.google.com/books/edition/Psychedelic\_Integration/0AzdzgEACAAJ?hl=en.

<sup>74</sup> Hartogsohn, I., *Constructing drug effects: A history of set and setting.* Drug Science, Policy and Law, 2017. 3: p. 2050324516683325. Available from: <u>https://journals.sagepub.com/doi/abs/10.1177/2050324516683325</u>.

<sup>75</sup> Bourzat, F. and K. Hunter, *Consciousness Medicine: Indigenous Wisdom, Entheogens, and Expanded States of Consciousness for Healing Healing and Growth*. 2019: North Atlantic Books. Available from:

https://www.google.com/books/edition/Consciousness Medicine/eKltDwAAQBAJ?hl=en&gbpv=1&dq=Consciousn ess+Medicine:+Indigenous+Wisdom,+Entheogens,+and+Expanded+States+of+Consciousness+for+Healing+Healing +and+Growth.&printsec=frontcover.

<sup>76</sup> Bathje, G.J., E. Majeski, and M. Kudowor, *Psychedelic integration: An analysis of the concept and its practice*. Front Psychol, 2022. 13: p. 824077. Available from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9386447/</u>.

<sup>77</sup> Butler, K. and J. Moore, *Integration Workbook*. 2023, Middletown: Psychedelics Today. Available from: <u>https://psychedelicstodayshop.com/products/integration-workbook-ebook</u>.

<sup>78</sup> Johnston, C.B., et al., *The Safety and Efficacy of Psychedelic-Assisted Therapies for Older Adults: Knowns and Unknowns.* Am J Geriatr Psychiatry, 2023. 31(1): p. 44-53. Available from: https://pubmed.ncbi.nlm.nih.gov/36184377/.

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