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REVIEW ARTICLE

Neurobiological and Therapeutic Potential of Psilocybin in Psychiatric Disorders

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Abstract: Psilocybin, an indoleamine alkaloid derived from various fungal species, is the subject of renewed, rigorous investigation for its therapeutic potential in psychiatry. This compound, a prodrug for the active metabolite psilocin, functions primarily as a partial agonist at the serotonin 2A (5-HT2A) receptor. Its administration within a structured psychotherapeutic context is associated with rapid and sustained antidepressant and anxiolytic effects, particularly in populations with treatment-resistant depression and existential distress related to life-threatening illnesses. The neurobiological mechanisms are multifaceted, initiated by acute 5-HT2A-mediated disruption of key brain networks, most importantly the Default Mode Network (DMN). This network destabilization correlates with subjective experiences of ego dissolution and is hypothesized to create a state of elevated brain entropy. This acute phase is followed by a period of enhanced neuroplasticity, driven by downstream signaling pathways involving BDNF and mTOR, which promotes synaptogenesis and dendritic spine growth in cortical neurons. This "window of plasticity" may facilitate the unlearning of maladaptive cognitive patterns and the formation of new, adaptive associations. Clinical trials demonstrate significant efficacy, though psychological risks necessitate careful screening, preparation, and a supportive therapeutic environment. The translation of psilocybin-assisted therapy from research to clinical practice presents challenges related to protocol optimization, clinician training, and scalability.

Keywords: Psilocybin; Psilocin; Serotonin 2A Receptor; Neuroplasticity; Major Depressive Disorder

1. Introduction

Mental health disorders, including major depressive disorder (MDD), anxiety disorders, and substance use disorders (SUDs), constitute a significant and increasing global health burden [1]. Conventional pharmacological interventions, such as selective serotonin reuptake inhibitors (SSRIs), represent the first line of treatment for many. However, these medications possess notable limitations, including a delayed onset of therapeutic action, often requiring weeks or months to achieve full effect. Moreover, a substantial portion of patients, particularly those with treatment-resistant depression (TRD), fail to achieve adequate remission, and many experience undesirable side effects that impede long-term adherence [2]. This therapeutic gap has spurred investigation into novel treatment modalities with distinct mechanisms of action. In this context, the classic psychedelic compound psilocybin has re-emerged as a molecule of significant interest in neuropsychiatry. Psilocybin (4-phosphoryloxy-N,N-dimethyltryptamine) is a naturally occurring indoleamine alkaloid found in over 200 species of fungi, principally within the genus *Psilocybe* [3]. The use of these fungi is not novel; they have a long history in Mesoamerican indigenous cultures, where they were employed in spiritual and healing ceremonies long before their introduction to Western science [4].

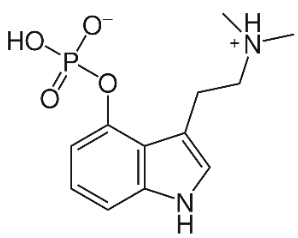

Figure 1. Structure of Psilocybin

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The modern scientific investigation of psilocybin began in the mid-20th century after its isolation and synthesis by Albert Hofmann in 1958 [5]. Early research during the 1950s and 1960s explored its potential for various conditions, including alcoholism and end-of-life anxiety [6]. However, this line of inquiry was abruptly halted by socio-political shifts, culminating in the classification of psilocybin as a Schedule I substance under the 1970 U.S. Controlled Substances Act, which severely restricted research for decades [7]. A renaissance in psychedelic science has occurred in the 21st century, characterized by methodologically rigorous clinical trials. This resurgence has been bolstered by regulatory shifts; the U.S. Food and Drug Administration (FDA) has granted psilocybin "Breakthrough Therapy" designation for both TRD (2018) and MDD (2019), expediting its development as a potential treatment [8].

Psilocybin's psychoactive effects are mediated by its active metabolite, psilocin (4-hydroxy-N,N-dimethyltryptamine). Following ingestion, psilocybin is rapidly dephosphorylated to psilocin, which readily crosses the blood-brain barrier [9]. Psilocin acts as a partial agonist at multiple serotonin receptors, but its profound psychological effects are primarily attributed to stimulation of the serotonin 2A (5-HT2A) receptor [10]. Modern neuroimaging studies suggest this 5-HT2A agonism leads to a profound, acute alteration of brain network dynamics. An important finding is the disintegration of the Default Mode Network (DMN), a network associated with self-referential thought, which correlates with the subjective experience of "ego dissolution" [11]. This acute network disruption is followed by a downstream, sustained promotion of neuroplasticity, potentially mediated by Brain-Derived Neurotrophic Factor (BDNF) [12]. This cascade is hypothesized to create a temporary "window of plasticity," allowing for the revision of maladaptive cognitive and emotional patterns. The main objective of this review is to explain the current state of knowledge regarding psilocybin, focusing on its pharmacology, neurobiological mechanisms, and the clinical evidence for its therapeutic use.

2. Chemistry, Biosynthesis, and Pharmacology

2.1. Chemical Structure and Biosynthesis

Psilocybin is a tryptamine derivative, structurally similar to the endogenous neurotransmitter serotonin (5-HT). Its biosynthesis in *Psilocybe* fungi, a pathway that was enigmatic for decades, has recently been elucidated. It involves a four-step enzymatic cascade that converts the primary metabolite L-tryptophan into psilocybin. The pathway begins with the decarboxylation of L-tryptophan to tryptamine by the enzyme PsiD. Subsequently, the enzyme PsiH, a monooxygenase, hydroxylates tryptamine at the 4-position of the indole ring to produce 4-hydroxytryptamine (norbaeocystin). The kinase PsiK then phosphorylates this intermediate to form baeocystin. In the final step, the methyltransferase PsiM catalyzes the iterative N-methylation of baeocystin, using S-adenosyl-L-methionine (SAM) as a methyl donor, to yield psilocybin [13]. The genes encoding this enzymatic cluster (*psiD*, *psiH*, *psiK*, *psiM*) have been identified, opening pathways for the biotechnological production of psilocybin in heterologous hosts, such as *Saccharomyces cerevisiae* or *Escherichia coli*, which allows for scalable and consistent synthesis independent of fungal cultivation [14].

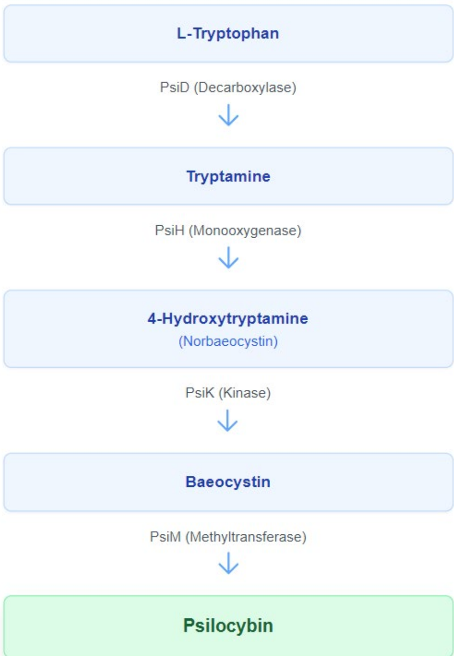

Figure 2. Enzymatic Biosynthesis of Psilocybin

2.2. Pharmacokinetics

Psilocybin itself is pharmacologically inert and functions as a prodrug. Upon oral ingestion, it undergoes rapid dephosphorylation, primarily by alkaline phosphatases in the intestine and liver, to its active, lipophilic metabolite, psilocin [9, 15].

Absorption of orally administered psilocybin is relatively rapid, with peak plasma concentrations (Cmax) of psilocin typically observed between 60 and 120 minutes (Tmax) post-administration. Clinical protocols often recommend fasting prior to administration to ensure more consistent absorption and predictable onset of effects [16]. Psilocin is highly lipophilic, allowing it to efficiently cross the blood-brain barrier and distribute widely throughout body tissues.

Table 1. Pharmacokinetic Profile of Psilocybin and Psilocin

Parameter	Description	Characteristic
Drug Form	Psilocybin	Prodrug (4-phosphoryloxy-N,N-dimethyltryptamine)
Active Metabolite	Psilocin	Active (4-hydroxy-N,N-dimethyltryptamine)
Conversion	Dephosphorylation	Rapidly occurs via alkaline phosphatases (intestine, liver)
Bioavailability (Oral)	N/A (Psilocin)	~50-60% (Estimated)
Tmax (Peak Plasma)	Psilocin (post-psilocybin)	60 - 120 minutes
T½ (Elimination)	Psilocin	2 - 3 hours
Primary Metabolism	Psilocin	Glucuronidation (via UGT1A9 and UGT1A10) to psilocin-O-glucuronide (inactive)
Primary Excretion	Psilocin-O-glucuronide	Renal (Urine)
Duration of Effects	Subjective psychological	4 - 6 hours

The metabolism of psilocin is the primary route of its elimination. It is extensively metabolized in the liver, mainly through glucuronidation by UDP-glucuronosyltransferase (UGT) enzymes, particularly UGT1A9 and UGT1A10, to form the inactive metabolite psilocin-O-glucuronide. A minor fraction is oxidized by monoamine oxidase (MAO) [17]. The elimination half-life (T½) of psilocin is relatively short, approximately 2 to 3 hours. The majority of the dose is excreted renally as psilocin-O-glucuronide within 24 hours. This pharmacokinetic profile aligns with the typical duration of subjective psychoactive effects, which generally last between 4 and 6 hours [16].

2.3. Pharmacodynamics

The pharmacodynamic actions of psilocin are central to its psychological and therapeutic effects. Psilocin is a non-selective serotonergic agonist with affinity for multiple 5-HT receptor subtypes. However, its potent, partial agonist activity at the 5-HT2A receptor is the primary mediator of its psychedelic properties [10]. This has been demonstrated in human studies where pre-treatment with a 5-HT2A antagonist, such as ketanserin, effectively blocks the subjective and neurophysiological effects of psilocybin [18]. Psilocin also binds with notable affinity to other receptors, including 5-HT1A, 5-HT2B, 5-HT2C, and 5-HT7, which may modulate the qualitative aspects of the experience and contribute to its broader therapeutic profile [19].

Table 2. Receptor Binding Profile of Psilocin

Receptor Target	Receptor Type	Function	Binding Affinity (Ki)
5-HT2A	Serotonin (Gq-coupled)	Primary psychedelic mediator. High-order cognition, perception, mood.	High (~6 nM)
5-HT1A	Serotonin (Gi-coupled)	Modulates mood, anxiolytic effects.	Moderate (~128 nM)
5-HT2C	Serotonin (Gq-coupled)	Modulates mood, appetite, dopamine release.	Moderate (~45 nM)
5-HT7	Serotonin (Gs-coupled)	Involved in cognition, circadian rhythm, and mood.	Moderate-High
5-HT2B	Serotonin (Gq-coupled)	Peripherally involved in cardiac valve function; central role less clear.	Moderate

3. Neurobiological Mechanisms of Action

The therapeutic outcomes of psilocybin-assisted therapy are thought to result from a cascade of neurobiological events, beginning with acute receptor-level actions that translate into large-scale network changes, followed by sustained molecular processes that enhance neuroplasticity.

3.1. 5-HT2A Receptor Agonism

The primary target of psilocin, the 5-HT2A receptor, is densely expressed on the apical dendrites of layer V pyramidal neurons, particularly in high-order association cortices such as the prefrontal cortex (PFC) and posterior cingulate cortex (PCC) [20]. These regions are critical hubs of brain networks involved in cognition and self-referential processing.

Psilocin's binding to these receptors activates the Gq-mediated signaling pathway, leading to an increase in intracellular calcium and the potentiation of glutamate release from thalamic inputs [21]. This results in an excitatory, desynchronizing effect on cortical pyramidal neurons, disrupting their typical, constrained firing patterns.

Functional Magnetic Resonance Imaging (fMRI) studies have visualized the large-scale consequences of this neuronal disruption. A consistent finding is the acute "disintegration" or desynchronization of the Default Mode Network (DMN) [11, 22]. The DMN is a highly integrated network that is most active during wakeful rest and is associated with self-referential thought, rumination, and autobiographical memory. The magnitude of DMN disintegration during the psilocybin experience correlates strongly with subjective reports of "ego dissolution," or a dissolution of the boundary between self and environment [22].

Concurrently, while established networks like the DMN become less integrated, the brain enters a state of increased global functional connectivity. Communication is enhanced between brain networks that are normally distinct or anti-correlated, creating a more fluid and hyper-associative state of consciousness [23]. The "entropic brain" hypothesis posits that psilocybin temporarily increases the entropy (randomness or flexibility) of brain activity, shifting the system from the rigid, predictable patterns characteristic of disorders like depression into a more flexible state that is receptive to change [24].

Figure 3. The Entropic Brain Hypothesis in Depression

3.2. Sustained Effects on Neuroplasticity

While the acute network disruption provides a window for change, the long-term therapeutic benefits are hypothesized to be consolidated by the promotion of neuroplasticity. This "secondary" mechanism allows for the structural and functional rewiring of neural circuits.

This process is also initiated by 5-HT2A agonism. The resulting increase in glutamatergic activity, particularly through AMPA and NMDA receptors, triggers downstream intracellular cascades. A key pathway involves the stimulation of Brain-Derived Neurotrophic Factor (BDNF) synthesis and release [12]. BDNF binds to its high-affinity receptor, Tropomyosin receptor kinase B (TrkB), activating signaling pathways crucial for neuronal growth and survival [25].

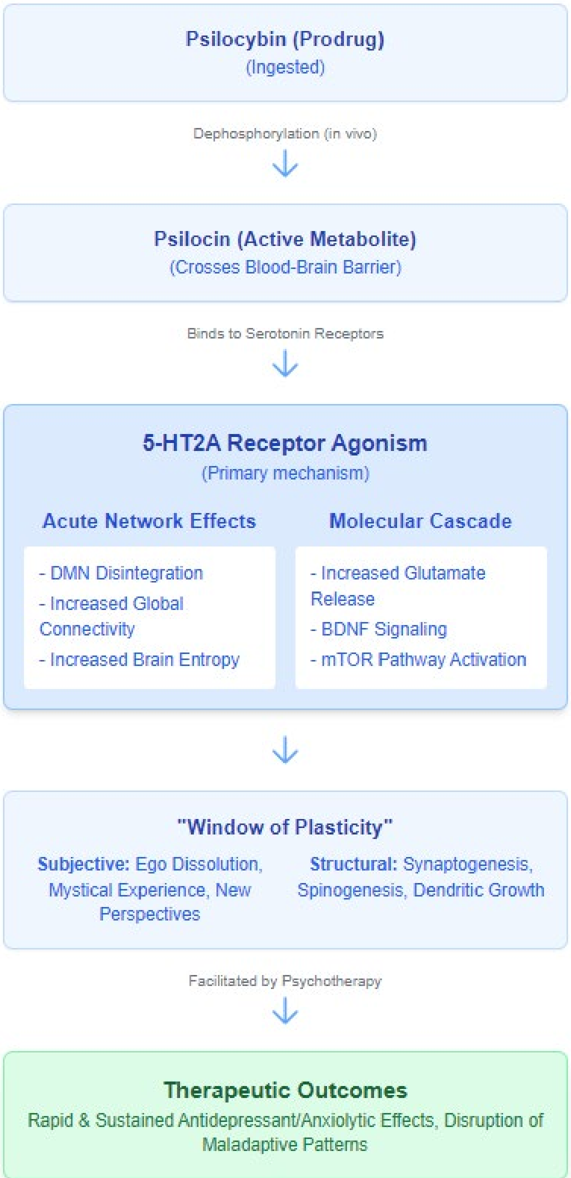

Figure 4. Proposed Neurobiological Mechanism of Psilocybin

One of the principal pathways activated by BDNF-TrkB signaling is the mammalian Target of Rapamycin (mTOR) pathway [26]. mTOR is a master regulator of protein synthesis, and its activation is essential for synaptogenesis—the formation of new synaptic connections. This cascade ultimately leads to the transcription of genes necessary for structural plasticity.

Preclinical studies provide direct evidence for these structural changes. Administration of psilocybin or psilocin in animal models has been shown to rapidly and durably increase the density of dendritic spines (spinogenesis) and promote the growth of new dendritic branches (dendritogenesis) on pyramidal neurons in the cortex [12, 27]. These structural enhancements, which represent the formation of new synapses, are observed within 24 hours of administration and can persist for at least one month. This period of enhanced plasticity is theorized to be the critical temporal window during which psychotherapy can be most effective, allowing the patient to consolidate new insights and form healthier cognitive and emotional patterns, effectively unlearning the rigid, ruminative pathways that characterize depression [28].

4. Clinical Applications in Psychiatry

Psilocybin is not administered as a standalone medication. Its efficacy is evaluated within the context of a structured protocol known as Psilocybin-Assisted Therapy (PAT). This model is fundamental to its clinical application and safety.

4.1. The Psilocybin-Assisted Therapy (PAT) Model

The PAT model consists of three distinct phases. First is the preparation phase, involving several sessions where two trained therapists build rapport and a strong therapeutic alliance with the patient. They provide education about the potential effects of psilocybin, establish safety protocols, and work with the patient to set intentions for the experience. Second is the dosing session, which lasts 6-8 hours. The patient receives a measured dose of psilocybin in a comfortable, controlled, living-room-like environment. They are typically encouraged to wear eyeshades and listen to a curated music playlist to facilitate an inward-directed experience, while the therapists provide continuous, non-directive support. Third is the integration phase, consisting of one or more psychotherapy sessions in the days and weeks following the dosing session. In this phase, therapists help the patient process, interpret, and make meaning of their experience, translating psychological insights into tangible changes in their life and behavior [29].

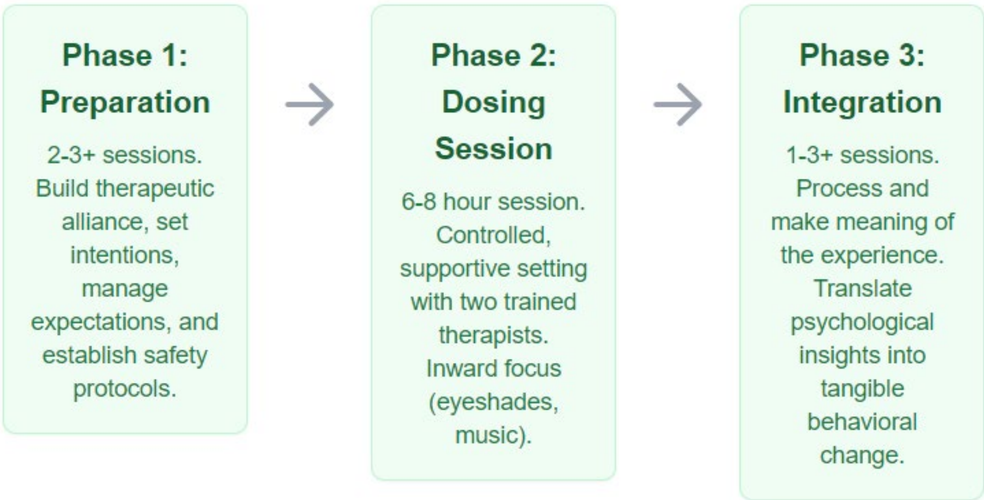

Figure 5. The Psilocybin-Assisted Therapy (PAT) Clinical Model

4.2. Depressive and Anxiety Disorders

4.2.1. Cancer-Related Existential Distress

Some of the most compelling modern evidence for psilocybin therapy comes from studies with patients experiencing profound depression and anxiety related to a life-threatening cancer diagnosis. Two landmark randomized controlled trials (RCTs) conducted in 2016 demonstrated remarkable effects. One study, led by Griffiths et al., involved 51 patients in a crossover design, comparing a high dose of psilocybin with a very low, active control dose. The high dose produced immediate, substantial, and sustained decreases in measures of depression, anxiety, and death anxiety, along with increases in quality of life and optimism. At the 6-month follow-up, approximately 80% of participants continued to show clinically significant reductions in symptoms [30]. A similar RCT by Ross et al. with 29 patients found comparable results, with 60-80% of participants demonstrating sustained benefits at 6.5 months [16]. In both studies, the intensity of the mystical-type experience during the session was a key mediator of the positive therapeutic outcome.

4.2.2. Treatment-Resistant Depression (TRD)

TRD, defined as MDD that has not responded to two or more adequate trials of conventional antidepressants, is a major clinical challenge. Psilocybin has shown significant promise in this population. The largest RCT to date, published by Goodwin et al. in 2022, was a multi-site, double-blind trial involving 233 patients with TRD. Participants were randomized to receive a single 25 mg, 10 mg, or 1 mg (control) dose of psilocybin with psychological support. The 25 mg dose group showed a highly statistically significant and clinically relevant reduction in depressive symptoms at 3 weeks compared to the 1 mg control group. The effect was rapid, with improvements seen one day after dosing, and was sustained for many responders at 12 weeks [31].

4.2.3. Major Depressive Disorder (MDD)

Apart from TRD, psilocybin has been compared directly against a standard antidepressant. A 2021 RCT by Carhart-Harris et al. randomized 59 patients with moderate-to-severe MDD to receive either two 25 mg doses of psilocybin three weeks apart or a 6-week course of the SSRI escitalopram. The study found that while psilocybin was not statistically superior on the primary outcome measure, psilocybin-assisted therapy was at least as effective as escitalopram. Moreover, the psilocybin group showed significantly greater improvements on several secondary outcomes, including remission rates, well-being, and a reduction in emotional blunting [32]. A prior waitlist-controlled trial by Davis et al. in 2021 also demonstrated that two doses of psilocybin produced rapid and large reductions in depressive symptoms, with 71% of participants showing a clinically significant response at 4 weeks [33].

4.3. Substance Use Disorders

Preliminary research suggests psilocybin therapy may be effective in disrupting addictive patterns. A pilot study from Johns Hopkins University for tobacco smoking cessation found that psilocybin-assisted therapy, combined with cognitive-behavioral therapy, produced an 80% abstinence rate at a 6-month follow-up, a rate far exceeding those of standard smoking cessation treatments [34]. Similarly, a trial in patients with alcohol use disorder found that two doses of psilocybin significantly reduced the percentage of heavy drinking days and alcohol cravings compared to an active placebo group [35].

Table 3. Clinical Trials for Psilocybin-Assisted Therapy (PAT)

Study	Condition	Design	N	Intervention	Comparator	Findings
Griffiths et al. [30]	Cancer-Related Distress	RCT, Crossover	51	High-dose psilocybin (22 or 30 mg/70kg)	Very low-dose psilocybin (1 or 3 mg/70kg)	Immediate, substantial, and sustained (>6 mos) decreases in depression and anxiety. Mystical experience mediated outcome.
Ross et al. [16]	Cancer-Related Distress	RCT, Parallel	29	Single moderate-high dose psilocybin (0.3 mg/kg)	Niacin (Active Placebo)	~80% of participants showed sustained anxiolytic/antidepressant effects at 6.5-month follow-up.
Goodwin et al. [31]	Treatment-Resistant Depression (TRD)	RCT, Multi-site	233	Single 25 mg dose psilocybin	Single 10 mg or 1 mg (control) dose	25 mg dose showed significant reduction in depressive symptoms at 3 weeks vs. 1 mg. Rapid onset of effect.
Carhart-Harris et al. [32]	Major Depressive Disorder (MDD)	RCT, Parallel	59	Two 25 mg doses psilocybin (3 weeks apart)	6-week course of Escitalopram (SSRI)	Psilocybin was non-inferior to escitalopram on primary outcome; superior on secondary outcomes (e.g., remission, well-being).
Davis et al. [33]	Major Depressive Disorder (MDD)	RCT, Waitlist Control	24	Two doses psilocybin	Waitlist control	Rapid and large reductions in depressive symptoms (71% response at 4 weeks).
Johnson et al. [34]	Tobacco Use Disorder	Pilot, Open-label	15	PAT with psilocybin	N/A (Compared to standard treatments)	80% smoking abstinence at 6-month follow-up.
Bogenschutz et al. [35]	Alcohol Use Disorder	RCT, Double-blind	93	Two doses psilocybin	Diphenhydramine (Active Placebo)	Psilocybin group showed significantly greater reduction in percentage of heavy drinking days.

4.4. Other Potential Applications

Research is expanding into other disorders characterized by rigid cognitive and behavioral patterns. Early-phase studies have suggested potential benefits for Obsessive-Compulsive Disorder (OCD), with participants reporting acute reductions in obsessions and compulsions following psilocybin administration [36]. Given the ego-syntonic and rigid nature of anorexia nervosa, psilocybin therapy is also being investigated as a potential intervention to address cognitive inflexibility and body-image distortion in this difficult-to-treat population [37].

5. Safety and Risk Mitigation

Despite its therapeutic promise, psilocybin is a potent psychoactive substance, and its use carries distinct risks that must be managed.

5.1. Physiological Safety

Psilocybin has a favorable physiological safety profile. It is not associated with organ toxicity, and there is no evidence of a lethal overdose in humans [38]. Its therapeutic index is estimated to be very high. The acute physical effects are generally mild and transient. These commonly include nausea (attributed to 5-HT3 receptor activation in the gut), mild and transient increases in blood pressure and heart rate, pupil dilation (mydriasis), and occasional headaches or dizziness [16, 30]. These effects are well-managed in a controlled clinical setting.

5.2. Psychological Risks

The primary risks of psilocybin are psychological. The most common is the induction of acute psychological distress during the session, often termed a "challenging experience" or "bad trip." This can manifest as intense anxiety, paranoia, panic, grief, or profound confusion and disorientation [39]. While these experiences can be frightening, in a therapeutic setting they are often navigated with therapist support and can lead to significant breakthroughs. However, in an unsupported or uncontrolled setting, they could lead to erratic or dangerous behavior.

Table 4. Adverse Effects and Psychological Risks

Category	Adverse Effect	Frequency
Physiological (Acute)	Nausea / Vomiting	Common (Often during onset)
	Mild Tachycardia	Common (Transient increase in heart rate)
	Mild Hypertension	Common (Transient increase in blood pressure)
	Headache	Common (Often post-session)
	Dizziness, Mydriasis (Pupil Dilation)	Common (During session)
Psychological (Acute)	Anxiety, Fear, Paranoia	Common; part of a "challenging experience." Manageable with therapeutic support.
	Confusion / Disorientation	Common; part of subjective psychedelic state.
	Grief, Dysphoria, Sadness	Common; often related to processing difficult emotions.
Psychological (Persistent)	Transient Psychosis	Rare; primarily a risk in predisposed individuals (e.g., history of psychosis).
	Hallucinogen Persisting Perception Disorder (HPPD)	Very rare; spontaneous re-experiencing of visual disturbances.

More serious, though rare, adverse events include the precipitation of transient psychotic episodes, particularly in vulnerable individuals. A rare, long-term risk is Hallucinogen Persisting Perception Disorder (HPPD), a poorly understood condition characterized by the re-experiencing of visual disturbances long after the drug has been eliminated [40].

5.3. Contraindications and Risk Mitigation

The PAT model is itself the primary risk mitigation strategy. This begins with comprehensive screening. Key contraindications for clinical trials include a personal or first-degree family history of a psychotic disorder (e.g., schizophrenia) or bipolar I disorder, as psilocybin could unmask or exacerbate these conditions. The preparation phase, which builds trust and educates the patient, is critical for reducing fear and providing tools to navigate difficult experiences. The continuous, non-directive support from trained therapists during the dosing session provides a "safety container" to ensure the patient's physical and psychological security. Finally, the integration phase helps to contextualize and resolve any distressing content from the experience, transforming it into meaningful insight [29, 39]

Table 5. Contraindications and Risk Mitigation Measures in Psilocybin-Assisted Therapy (PAT)

Category	Strategy / Factor	Rationale
Contraindications	Personal or first-degree family history of a psychotic disorder (e.g., Schizophrenia)	High risk of precipitating a first-episode or exacerbating an existing psychotic disorder.
	Personal or first-degree family history of Bipolar I Disorder	High risk of precipitating a manic episode.
	Uncontrolled cardiovascular conditions	Transient increases in blood pressure and heart rate could pose a risk.
Mitigation (Preparation)	Comprehensive psychiatric and medical screening	To identify and exclude high-risk (contraindicated) participants.
	Building therapeutic alliance / rapport	To establish trust, which is critical for navigating challenging experiences.
	Education and intention setting	To manage expectations, reduce fear of the unknown, and provide a therapeutic focus.
Mitigation (Dosing Session)	Two trained therapists / guides	To provide continuous, non-directive psychological support and ensure physical safety.
	Safe, comfortable, controlled environment	To minimize external stressors and prevent dangerous behavior during disorientation.
	Reassurance and grounding techniques	To help the patient navigate challenging psychological content without pharmacological intervention.
Mitigation (Integration)	Follow-up psychotherapy sessions	To process insights, contextualize difficult experiences, and translate insights into lasting behavioral change.

6. Conclusion

The evidence accumulated over the past two decades indicates that psilocybin, when administered within a structured psychotherapeutic framework, can catalyze rapid, substantial, and sustained improvements in symptoms for several difficult-to-treat psychiatric disorders. Its mechanism, which appears to involve a "reset" of brain network function followed by a period of enhanced neuroplasticity, offers a novel paradigm for mental healthcare that is distinct from conventional daily pharmacotherapy. The safety profile is manageable, with primary risks being psychological rather than physiological. Large-scale, multi-site Phase III trials are necessary to confirm the efficacy and safety of psilocybin for MDD and TRD and to achieve regulatory approval. Research must also refine clinical protocols, including determining optimal dosing, the necessary components of the accompanying therapy, and predictors of response. These include developing standardized, scalable training programs for therapists, navigating the high cost and resource-intensive nature of the PAT model to ensure equitable access, and continuing to educate the public and medical community to separate the therapeutic use of psilocybin from its recreational misuse. Research into non-hallucinogenic analogs that may retain the neuroplastic and antidepressant properties of psilocybin is also a promising frontier, which could potentially offer a more scalable intervention.

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