



Psychedelic Mushrooms: The Use of Psilocybin in the Treatment of Mental Disorders

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Abstract

Psychedelics are a class of hallucinogenic drugs. They have been explored particularly for treatment-resistant psychiatric illnesses. In recent years, advances in psychopharmacology have benefited thousands of patients with some type of mental disorder. Preliminary evidence has shown that psilocybin has shown promise in the treatment of psychiatric disorders, with the support of qualified doctors. Recent clinical studies have reported marked improvements in mental health in psilocybin-assisted psychotherapy. In many studies, the safety and efficacy of psilocybin have been the primary objectives to show that it is a safe and valid therapeutic alternative to other forms of psychiatric medications. Currently, some studies prove that psilocybin is safe in a controlled environment. However, the use of psilocybin needs to be further studied to determine the efficacy and safety of potential applications in medicine.

Keywords: Mushroom; Psychedelic; Psilocybin; Antidepressant; Mental Disorder

Abbreviations: WHO: World Health Organization; FDA: Food and Drug Administration; MDD: Major Depression Disorder; OCD: Obsessive-Compulsive Disorder; TRD: Treatment-Resistant Depression.

Introduction

Psychedelics are a class of hallucinogenic drugs that alter consciousness by acting on serotonin receptors in the brain. They have been explored as an alternative treatment, particularly for treatment-resistant psychiatric illnesses [1].

Mental disorder is characterized by a clinically significant disturbance in an individual's cognition, emotional or behavioral regulation. According to the World Health Organization, 1 in 8 people, or 970 million people worldwide, live with a mental disorder, with anxiety and

depressive disorders being the most common [2].

In 2020, the number of people living with anxiety and depressive disorders increased significantly due to the COVID-19 pandemic. Although there are effective prevention and treatment options, most people with mental health disorders do not have access to effective care. Many people also experience stigma, discrimination and human rights violations [2].

In recent years, advances in psychopharmacology have benefited thousands of patients with some type of mental disorder. Psychiatric medications can help lessen symptoms, however, their benefits for some are disappointing and their side effects from daily and long-term use can be problematic [3].

Preliminary evidence has shown that psilocybin has shown promise in the treatment of psychiatric disorders, with the support of trained doctors [4]. Clinical trials showed satisfactory results, resulting in a decrease in the severity of depressive symptoms [5].

Despite being classified as a Class I drug in the USA, the growing interest in the therapeutic potential of psychedelic drugs in recent years is currently notable. On July 23, 2023, the Food and Drug Administration (FDA) issued draft guidance to researchers and new drug sponsors for designing clinical trials for psychedelic drugs [6].

Psychoactive Mushrooms

Psilocybin is the main active ingredient of “magic mushrooms” of the genus *Psilocybe*, first identified in 1958 and synthesized in 1959 by Albert Hofmann [7]. Psilocybin and its dephosphorylated active metabolite, psilocin, are indole alkaloids that have a recognized hallucinogenic action. After oral ingestion, psilocybin is dephosphorylated to generate the phenol compound psilocin, crossing the blood-brain barrier and acts as a serotonin inhibitor, creating hallucinations and lasting beneficial changes in the brain, which in turn mediates its antidepressant and anxiolytic effects [8].

Psychedelic-assisted therapy has been gaining ground in recent years, after being decriminalized in the early 1960s despite promising initial research [9]. The resurgence of psychedelics began as therapeutic tools for resistant depression, particularly classic psychedelics such as psilocybin [10].

Therapeutic Use

Psilocybin is an alternative therapeutic tool for major depression disorder (MDD), obsessive-compulsive disorder, anorexia nervosa, post-traumatic stress disorder, cluster headache, chronic pain, and substance abuse (e.g., alcohol, cocaine, nicotine) [11-13].

Although more research is needed to evaluate the efficacy and safety in the treatment of mental disorders, a series of studies carried out decades ago with psilocybin have shown substantial reductions in anxiety, improved mood and improved quality of life in patients [14].

Recent clinical studies have reported marked improvements in mental health in psilocybin-assisted psychotherapy [3,15]. Its antidepressant effect has been supported by several small studies in patients with cancer-related depression and patients with MDD or TRD and recently in a large double-blind randomized trial with 233

participants with ESRD [3,16-21].

Recent clinical trials have yielded positive results from a patented synthetic formulation of psilocybin (COMP360) being developed for treatment-resistant depression (TRD), defined as failure to respond to 2 to 4 evidence-based antidepressant medications. To date, their studies have been the pioneers in the multicenter and international randomized clinical trial, and the largest, in phase 2, with the participation of 233 patients with depression [4].

The results of the study by Rotz, et al. suggest that a single [22], moderate dose of psilocybin may be as effective in reducing depressive symptoms as the higher repeated doses administered in previous studies [3], while also inducing fewer adverse events.

In many studies, the safety and efficacy of psilocybin have been the primary objectives to show that it is a safe and valid therapeutic alternative to other forms of psychiatric medications. Randomized clinical trial, presented positive results after evaluating the efficacy and safety of psilocybin therapy in patients with depressive disorder [23] and the growing evidence as an adjuvant in the treatment of a variety of psychiatric conditions, such as depression and anxiety related cancer and treatment-resistant depression [18,20,24]. Therefore, the effectiveness of antidepressants goes beyond the symptoms of depression assessed by a doctor. Patients reported improvements in positive and negative affect, but the effects on quality of life and cognition were smaller [4].

Among psychedelic drugs, psilocybin has the most favorable safety profile. When prescribed to carefully vetted patients at recommended doses, psilocybin is remarkably safe. They do not present tissue toxicity, do not interfere with liver function, have few drug interactions and do not present long-term physical effects [25,26].

Larger and longer trials, including comparison with existing treatments, for mental disorders are needed to determine the efficacy and safety of psilocybin. The most frequent adverse events are headache, nausea, dizziness and fatigue [21]. In the review study conducted by Psiuk, et al. [27], psilocybin did not reveal any serious adverse effects during the administration period. However, for Goodwin et al. [21], on the 1st day of drug administration, there were no serious adverse events. From the 2nd day to the 3rd week, serious adverse events were observed in 17% of the group investigated.

Given these results, the response to psilocybin-assisted treatment demonstrated long-term safety. During the treatment follow-up period, there were no serious adverse

effects, suicidal ideation was low, and there were no cases of self-injurious behavior [23].

However, it is important to highlight the importance of more research that evaluates the safety of using this psychedelic. Although some studies have already explicitly reported these results [28], further studies are needed in both clinical and recreational settings.

Recently, the first multicenter randomized clinical trial using psilocybin therapy showed promising positive results for the treatment of depressive disorder. Therefore, the therapy has already been tested first in initial and final phase 2 trials for this disease [3,16,22].

Given these results, the authors suggest longer and larger trials, including comparison with existing treatments for depression, are needed to determine the efficacy and safety of psilocybin for treatment-resistant depression [21].

Therefore, phase 3 clinical trials are currently underway to investigate the safety of the psychedelic in people suffering from the psychological disorder [29]. Furthermore, the precise dose and concentration of the psychedelic substance required in treatment to achieve therapeutic benefit have not yet been defined through scientific evidence. Therefore, it is important to advance future studies with clinical trials that can guarantee safety for patients with some type of depressive disorder.

Conclusion

This study investigated that psilocybin may be effective in reducing the symptoms of mental disorders, such as depression, suicide and others. Whereas, there are a limited number of randomized or controlled clinical trials. Thus, there is a need for more research, to rule out its efficacy and safety. Currently, some studies prove that psilocybin is safe in a controlled environment, and administered in low doses, patients demonstrate significant improvement in symptoms in some psychiatric illnesses. However, the use of psilocybin needs to be further studied to determine the efficacy and safety of potential applications in medicine.

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