

Psilocybin in the Treatment of Depression

Authors: Ben Hoelscher, PharmD Candidate 2022, Ronald Worthington, PhD

Abstract

Depression is a common condition with potentially fatal and debilitating consequences. Development of novel and efficacious agents for the treatment of depression has been relatively stagnant. The pathophysiology of depression remains unclear. The monoamine hypothesis is the most widely accepted model of explanation. The vast majority of antidepressants in use were developed targeting monoaminergic neurotransmission. There is no standard prescribing algorithm for depression treatment, and these agents do not provide adequate relief for all patients. Efficacy of antidepressants observed in clinical trials can be heavily influenced by non-specific factors such as expectancy and therapeutic alliance. Initial treatment failure is common as well as eventual relapse of depressive symptoms. Discontinuation of antidepressant therapy due to side effect burden is also a common occurrence. Psilocybin has become an agent of interest in the treatment of depression. The exact mechanism of action with psilocybin therapy in depression is not known. However, existing studies support increases in cortical neuroplasticity and long-term changes in network functionality as being key components. Psilocybin has historically been viewed as a dangerous compound with a high potential for abuse. Existing research supports psilocybin as being a safe therapy option when administered under direct medical supervision in patients without psychotic disorders or a predisposition to psychotic disorders. Recent studies have demonstrated safety and efficacy with no severe adverse reactions or dependence recorded. Research of this agent has resulted in novel study design and outcome measures not found in traditional antidepressant clinical trials.