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Making ShROOM for Psilocybin in the Treatment of Depressive Disorders

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Disclosure

- **Relevant Financial Conflicts of Interest**
  - **CE Presenter, Erin Price, PharmD**
    - None
  - **CE Mentor, Brianne Wolfe, PharmD, BCCCP**
    - None
- **Off-Label Uses of Medications**
  - Psilocybin

Outline

1. Background
2. Pharmacologic properties
3. Toxicity
4. Interactions
5. Literature review

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Abbreviations

- **5-HT:** 5-hydroxytryptamine
- **CI:** confidence interval
- **FDA:** Federal Drug Administration
- **LD50:** lethal dose, 50%
- **LSD:** lysergic acid diethylamide
- **MAO:** monoamine oxidase
- **MDD:** major depressive disorder
- **MDMA:** 3,4-methylenedioxymethamphetamine
- **RCT:** randomized controlled trial
- **SD:** standard deviation
- **SNRI:** serotonin-norepinephrine reuptake inhibitor
- **SSRI:** selective serotonin reuptake inhibitor
- **TRD:** treatment-resistant depression
- **UGT:** UDP-glucuronosyltransferase

Learning Objectives – Pharmacists

- Describe the pharmacologic and pharmacokinetic characteristics of psilocybin
- Recognize common adverse effects associated with psilocybin
- Analyze potential psilocybin drug interactions
- Assess clinical trials evaluating the antidepressive effects of psilocybin
- Apply knowledge of psilocybin clinical trial design to a patient case

Learning Objectives – Technicians

- Identify the mechanism of action of psilocybin
- Recognize common adverse effects associated with psilocybin
- Distinguish drug classes that may interact with psilocybin
- Examine the role of psychotherapy in clinical trials evaluating psilocybin

Background

Depressive Disorders – Definitions

- **MDD:**
  - 5 or more symptoms related to depressed mood or loss of interest during the same 2-week period
- **TRD:**
  - MDD that has not responded to 2 or more adequate trials of medications
- **Treatment response:**
  - 50% or greater reduction in depression severity from baseline

Department of Veterans Affairs, Department of Defense. VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder. *The Management of Major Depressive Disorder Working Group.* Published online 2022.

Background – Depressive Disorders

Epidemiology

- 20% of the US population experience MDD in their lifetimes
- Depression affects up to 20% of patients living with cancer
- Death by suicide is the 12th leading cause of death in the US

Treatment consists of SSRIs, SNRIs, or other agents, used with cognitive behavioral therapy

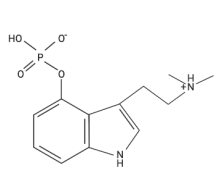
- Response to first-line therapy achieved in ~40-60% of patients
- An estimated 10-30% of patients who fail to respond to initial therapy will remain resistant to other treatments

Qaseem A, Owens DK, Etxeandia-Ikobaltzeta I, et al. Nonpharmacologic and Pharmacologic Treatments of Adults in the Acute Phase of Major Depressive Disorder: A Living Clinical Guideline From the American College of Physicians (published online ahead of print, 2023 Jan 24). *Ann Intern Med*. 2023;10.7326/M22-2056. doi:10.7326/M22-2056.
Pitman A, Suleman S, Hyde N, Hodgkiss A. Depression and anxiety in patients with cancer. BMJ. 2018;361:k1415. Published 2018 Apr 25. doi:10.1136/bmj.k1415.

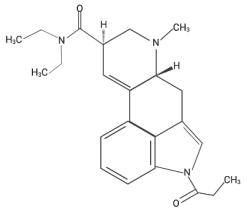
What Are Psychedelics?

- Agents that produce alterations in cognition, perception, and mood

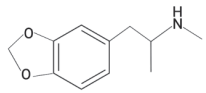
Tryptamines | **Lysergamides** | **Phenylethylamines**



Psilocybin



LSD



MDMA

Neavyn MJ, Carey JL. Hallucinogens. In: Nelson LS, Howland M, Lewin NA, Smith SW, Goldfrank LR, Hoffman RS. eds. Goldfrank's Toxicologic Emergencies, 11e. McGraw Hill; 2019.
Images created with BioRender.com (2023).

What is Psilocybin?

Simple tryptamine derived from *Psilocybe* mushrooms

Commonly Used Slang Names:

- "Magic Mushrooms"
- "Shrooms"

Waters K. Pharmacologic Similarities and Differences Among Hallucinogens. *J Clin Pharmacol*. 2021;61(S2). doi:10.1002/jcph.1917
Image: Lauterbach, L. "Psychedellic." *Flickr*, 18 Nov. 2006, https://www.flickr.com/photos/catarabbit/301452583/.

History of Psychedelic and Psilocybin Use

1579	Earliest documentation of psilocybin use in the *Florentine Codex*
1938	Sandoz Laboratories synthesizes LSD
1947	Sandoz begins marketing and distributing LSD for treatment of alcoholism and neurosis
1958	Psilocybin synthesized from dried sample of *Psilocybe* mushrooms
1960s	Sandoz distributes psilocybin product, Indocybin™
1970	Hallucinogens are prohibited following the enactment of the Controlled Substances Act
2004	Clinical trials for psilocybin resume after long hiatus
2019	Usona Institute granted FDA Breakthrough Therapy designation for psilocybin-based MDD treatment

Lowe H, Toyang N, Steele B, et al. The Therapeutic Potential of Psilocybin. *Molecules*. 2021;26(10). doi:10.3390/molecules26102948
Image: Farshore, L. "Hallucinogens." *Flickr*, 25 Mar. 2011, https://www.flickr.com/photos/50875151

Psilocybin Legislature

Listed as schedule I substance

- No currently accepted medical use and high potential for abuse

FDA Breakthrough Therapy designation

- Requested by drug manufacturers

Increasing number of legislative initiatives for psychedelic reform

- 90% of bills referred to psilocybin
- 14% of bills have been signed into law since 2019
  - CO, CT, HI, NJ, OR, TX, WA

The Third Psychedelic "Renaissance"

Drug manufacturers invested over $700 million in psychedelic product development in 2021

73 psilocybin studies actively registered with the National Institutes of Health in the United States

32 active psychedelic reform bills in 25 states

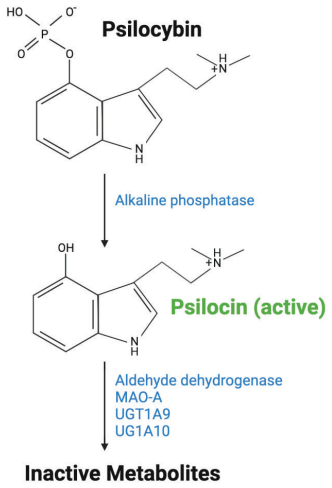
Pharmacologic Properties

Mechanism of Action

Psilocybin is a prodrug and requires conversion to its active metabolite, psilocin

Psilocin acts as a partial $5HT_{2A}$ receptor agonist

Psilocybin Bioactivation and Metabolism



Lowe H, Toyang N, Steele B, et al. The Therapeutic Potential of Psilocybin. *Molecules*. 2021;26(10). doi:10.3390/molecules26102948

Image created with BioRender.com (2023).

Potential Mechanisms in Depressive Disorders – Relevant Definitions

- **Mystical-Type Experience**
  - *"A sense of unity, or the experience of becoming one with all that exists."* (Stace 1960b)
  - Assessed using the Mystical Experience Questionnaire (MEQ)

4 Factors of MEQ	MEQ Question Example
1) Mystical	Sense of reverence
2) Positive Mood	Feelings of peace and tranquility
3) Space/Time	Experience of timelessness
4) Ineffability	Sense that the experience cannot be described adequately in words

- **Ego Dissolution or "Ego Death"**
  - *"Temporarily experiencing a complete loss of subjective self-identity."* (Griffiths 2008)

Barrett FS, Johnson MW, Griffiths RR. Validation of the revised Mystical Experience Questionnaire in experimental sessions with psilocybin. *Journal of Psychopharmacology*. 2015;29(11). doi:10.1177/0269881115609019
Ko K, Knight G, Rucker JJ, Cleare AJ. Psychedelics, Mystical Experience, and Therapeutic Efficacy: A Systematic Review. *Front Psychiatry*. 2022;13:917199. Published 2022 Jul 12. doi:10.3389/fpsyt.2022.917199.

Potential Mechanisms in Depressive Disorders

- Increased neuroplasticity from release of brain-derived neurotrophic factor
- Beneficial changes in the default mode network
- Psychedelics allow patients to achieve greater insight and make meaningful progress in psychotherapy

Rosenblat JD, Husain MI, Lee Y, et al. The Canadian Network for Mood and Anxiety Treatments (CANMAT) Task Force Report: Serotonergic Psychedelic Treatments for Major Depressive Disorder. Can J Psychiatry. 2023;68(1):5-21. doi:10.1177/07067437221111371.

Image created with BioRender.com (2023).

Pharmacokinetics

- Rapidly absorbed and distributed into tissue as psilocin
- Psilocin undergoes first-pass hepatic metabolism followed by glucuronidation
- Psilocin is excreted in the urine as psilocin glucuronide (inactive metabolite)

Half-Life	Onset of Action	Peak Effect	Duration of Action
2-3 hours	15-45 minutes	1-3 hours	4-8 hours

**Parameters are dose-dependent, data based on single moderate to high dose (~20-30 mg of psilocybin)*

Dodd S, Norman TR, Eyre HA, et al. Psilocybin in neuropsychiatry: a review of its pharmacology, safety, and efficacy. CNS Spectrums. 2022:1-11. doi:10.1017/S1092852922000888.

Pharmacodynamics

Partial activation of 5-HT_{2A} receptor leads to partial downstream intracellular signaling

Tolerance develops rapidly and cross-tolerance with other hallucinogens is possible

No evidence of psilocybin use leading to dependence or addiction

Schlag AK, Aday J, Salam I, Neill JC, Nutt DJ. Adverse effects of psychedelics: From anecdotes and misinformation to systematic science. *J Psychopharmacol.* 2022;36(3):258-272. doi:10.1177/02698811211069100.

Psilocybin Dosing

MACROdosing:

- Definition: consumption of hallucinogenic dose once
- Dose: ~20-30 mg of psilocybin
- Note: all clinical trials for depressive disorders have evaluated hallucinogenic doses of psilocybin

MICROdosing:

- Definition: consumption of sub-hallucinogenic dose, often at more frequent intervals
- Dose: < 1 mg of psilocybin
- Note: dose is often referred to in weight of dried mushrooms (~0.5 grams)

MacCallum CA, Lo LA, Pistawka CA, Deol JK. Therapeutic use of psilocybin: Practical considerations for dosing and administration. *Front Psychiatry.* 2022;13:1040217. Published 2022 Dec 1. doi:10.3389/fpsyt.2022.1040217.
Image used under license from Shutterstock.com

Toxicity

Adverse Effects – Common

- Headache, nausea, confusion, anxiety, paranoia, mydriasis
- Dose-dependent increases in blood pressure and heart rate

Psilocybin. In: Natural Medicines Database. Somerville (MA): Therapeutic Research Center; 2022 [cited: 18 Jan 2023]. Available from: https://naturalmedicines.therapeuticresearch.com.
Image created with BioRender.com (2023).

Serious Adverse Effects – Case Reports

2 cases of takotsubo cardiomyopathy

1 case of rhabdomyolysis, acute renal failure, and seizures

13 deaths following ingestion

- 1 from status epilepticus
- 7 as a result of falling or jumping from buildings
- 1 secondary to hypothermia
- 1 reported suicide with confirmed ingestion on autopsy
- 1 confirmed heroin overdose
- 1 after following with ecstasy and alcohol
- 1 cardiac arrest in a heart transplant recipient

USHP

Schlag AK, Aday J, Salam I, Neill JC, Nutt DJ. Adverse effects of psychedelics: From anecdotes and misinformation to systematic science. *J Psychopharmacol*. 2022;36(3):258-272. doi:10.1177/02698811211069100

van Amsterdam J, Opperhuizen A, van den Brink W. Harm potential of magic mushroom use: a review. *Regul Toxicol Pharmacol*. 2011;59(3):423-429. doi:10.1016/j.yrtph.2011.01.006

National Poison Control Data From 2006-2016

8,649 psilocybin exposures

- 3,875 patients (65.9%) treated/evaluated and released from the emergency department
- 717 patients (12.2%) managed at home
- 3 deaths

92% of patients required two or fewer types of treatment

- Benzodiazepines (17%)
- Other sedation (2.3%)
- Intravenous fluids (22.4%)

USHP

Leonard JB, Anderson B, Klein-Schwartz W. Does getting high hurt? Characterization of cases of LSD and psilocybin-containing mushroom exposures to national poison centers between 2000 and 2016. *J Psychopharmacol*. 2018;32(12):1286-1294. doi:10.1177/0269881118793086.

Image created with BioRender.com (2023).

Risk of Serotonin Syndrome

No documented cases of psilocybin causing serotonin syndrome alone or in combination with other agents that act on serotonin

Phenylethylamine psychedelics have been associated with higher risk

Expected psychedelic effects may overlap with symptoms of serotonin syndrome

Symptoms of **myoclonus, extreme hyperthermia, rigidity,** or symptoms that persist longer than expected duration may be signs of serotonin syndrome

USHP

Malcolm B, Thomas K. Serotonin toxicity of serotonergic psychedelics. *Psychopharmacology (Berl)*. 2022;239(6):1881-1891. doi:10.1007/s00213-021-05876-x

Other Potential Risks

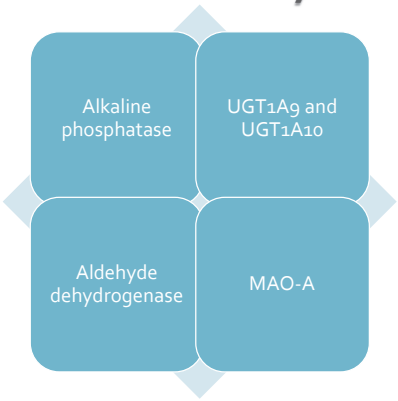
Overdose:	LD50 in rats: 280 mg/kg (roughly 7,000 times the dose used in studies)
Mushroom Toxicity:	Theoretical risk due to misidentification of mushrooms or consuming tainted illicit mushrooms
Long-Term Toxicity:	No documented adverse effects persisting beyond two weeks

USHP

Schlag AK, Aday J, Salam I, Neill JC, Nutt DJ. Adverse effects of psychedelics: From anecdotes and misinformation to systematic science. *J Psychopharmacol*. 2022;36(3):258-272. doi:10.1177/0269881121069100.

Drug and Disease Interactions

Enzymes Involved in Psilocybin Metabolism



Sarparast A, Thomas K, Malcolm B, Stauffer CS. Drug-drug interactions between psychiatric medications and MDMA or psilocybin: a systematic review. *Psychopharmacology (Berl).* 2022;239(6):1945-1976. doi:10.1007/s00213-022-06083-y

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Drug-Drug Interactions

Drug	Interaction	Outcome
Lithium	Unknown	Seizures
Diclofenac	UGT1A9/10 inhibition	Potentiation of psilocin effects
Probenecid	UGT1A9/10 inhibition	Potentiation of psilocin effects
Chlorpromazine	5-HT_{2A} receptor blockade	Attenuation of mydriasis, visual perception changes
Haloperidol	D2 receptor blockade	No effect on visual perception changes, worsening of ego dissolution dread
Risperidone	5-HT_{2A} receptor blockade	Attenuation of psilocybin-induced alterations in consciousness
Buspirone	5-HT_{1A} receptor agonism	Significant decrease in psychedelic effects of psilocybin
SSRIs	5-HT_{2A} receptor action	Blunting of psychedelic response
Stimulants	Additive adverse effects	Increase in blood pressure and heart rate
Estradiol products	Up-regulation of UGT1A9 expression	Theoretical increase in psilocin metabolism

Sarparast A, Thomas K, Malcolm B, Stauffer CS. Drug-drug interactions between psychiatric medications and MDMA or psilocybin: a systematic review. *Psychopharmacology (Berl).* 2022;239(6):1945-1976. doi:10.1007/s00213-022-06083-y

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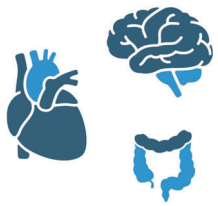
Drug-Disease Interactions



- Bipolar and schizophrenic disorders
- Cardiovascular disease
- Irritable bowel disease

Psilocybin. In: Natural Medicines Database. Somerville (MA): Therapeutic Research Center; 2022 [cited 2023 Jan 17]. Available from: https://naturalmedicines.therapeuticresearch.com. Subscription required to view.

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Literature Review

Overview

- Baseline depression therapies were tapered and discontinued before start of trials
- All studies utilized pharmaceutical grade psilocybin
- Psychotherapy or psychological support was incorporated in all study interventions
- Outcome measures varied between studies, but all are accepted in practice
- **Common exclusion criteria:**
  - Pregnant or breastfeeding
  - Personal or family history of psychotic disorder (1st and 2nd degree relatives)
  - History of, or current suicidal behavior

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Studies for Major Depressive Disorder or Treatment-Resistant Depression

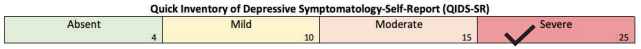
USHP

Image: Farshore, L. "Hallucinogens." *Flickr*, 25 Mar. 2011, https://www.flickr.com/photos/50875151

Carhart-Harris, et al. 2016

Design	Population	Intervention	Primary Outcome	Results
Open label feasibility study	Adults with TRD N = 12 Mean baseline QIDS-SR: 19.2	Psilocybin 10 mg, followed by 25 mg 7 days later Psychological support	Change in QIDS-SR from baseline to week 1 and month 3	QIDS-SR difference from baseline: **Week 1:** -11.8 (95% CI -9.15 to -14.35) p = 0.002 **Month 3:** -9.2 (95% CI -5.69 to -12.71) p = 0.003

- Goal was to assess the feasibility of administering psilocybin precluding large RCTs
- Participants were **not** required to stop baseline antidepressant medications before enrollment
- No comparator group
- Self-reported outcome



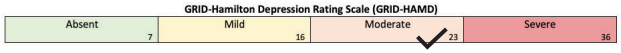
USHP

Carhart-Harris RL, Bolstridge M, Rucker J, et al. Psilocybin with psychological support for treatment-resistant depression: an open-label feasibility study. *Lancet Psychiatry*. 2016;3(7):619-627. doi:10.1016/S2215-0366(16)30065-7

Davis, et al. 2021

Design	Population	Intervention	Comparator	Primary Outcome	Results
RCT, wait list controlled	Age 21-75 with MDD N = 27 Mean baseline GRID-HAMD: 22.8	20 mg psilocybin, then 30 mg ~1.6 weeks later Psychotherapy	Wait list control (intervention delayed by 8 weeks)	Change in GRID-HAMD from baseline to week 1 and week 4	Mean GRID-HAMD (SD) (psilocybin): **Week 1:** 8.0 (7.1) **Week 4:** 8.5 (5.7) Mean GRID-HAMD (SD) (wait list): **Week 5:** 23.8 (5.4) **Week 8:** 23.5 (6.0)

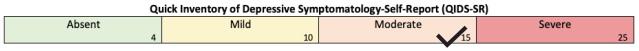
- All participants refrained from antidepressants for at least 5 half-lives before and up to 4 months after
- Session facilitators with varying degrees of clinical training
- Clinician-assessed outcome



Carhart-Harris, et al. 2021

Design	Population	Intervention	Comparator	Primary Outcome	Results
Double-blind RCT	Age 18-80 with MDD N = 59 Mean baseline QIDS-SR-16: 14.5	25 mg psilocybin (2 sessions, 3 weeks apart), then 3 weeks of placebo Psychological support	1 mg psilocybin (2 sessions, 3 weeks apart), then 3 weeks of escitalopram Psychological support	Change in QIDS-SR-16 from baseline to 6 weeks	Mean change in QIDS-SR-16 at 6 weeks: -8.0 in psilocybin group -6.0 in escitalopram group Between group difference of 2 points (p=0.17)

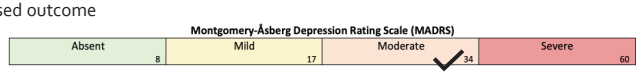
- Most patients self-referred for study entry
- No reports of serious adverse effects in either group
- Secondary outcomes could not be interpreted, but psilocybin was favored in each assessment
- Self-reported outcome



Goodwin, et al. 2022

Design	Population	Intervention	Comparator	Primary Outcome	Results
Double-blind RCT	Age ≥ 18 with TRD N = 233 Mean baseline MADRS: 32.5	25 mg psilocybin **or** 10 mg psilocybin Psychological support	1 mg psilocybin Psychological support	Change in MADRS from baseline to 3 weeks	Change in MADRS (**25 mg**): -6.6 (95% CI -10.2 to -2.9) p=<0.001 Change in MADRS (**10 mg**): -6.2 (95% CI -6.2 to 1.2) p=0.18

- Largest psilocybin clinical trial to date
- Patients were instructed not to restart antidepressants for at least 3 weeks after study
- Reports of adverse effects related to self injury or suicidal ideation/behavior higher in psilocybin groups
  - 25 mg group: 3 patients
  - 10 mg group: 2 patients
  - 1 mg group: 1 patient
- Clinician-assessed outcome



von Rotz, et al. 2022

Design	Population	Intervention	Comparator	Primary Outcome	Results
Double-blind RCT	Age 18-60 with MDD N = 52 Mean baseline MADRS: 24.3 BDI: 26.9	0.215 mg/kg psilocybin Psychotherapy	Placebo Psychotherapy	Change in symptom severity between visit 2 and visit 14 (MADRS, BDI)	**Change in MADRS:** -13.0 points (95% CI -15.0 to -1.3) p=0.0011 **Change in BDI:** -13.2 points (95% CI -13.4 to -1.3) p=0.019

- Patient population with less severe depression compared to other studies
- 19.2% of patients had history of previous psychedelic use versus 42.3% of patients in the placebo group
- Majority of patients in psilocybin group experienced substantial treatment-induced subjective effects
- Shortest follow-up period

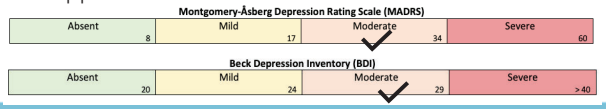


Image: Farshore, L. "Hallucinogens." *Flickr*, 25 Mar. 2011, https://www.flickr.com/photos/50875151

Grob, et al. 2011

Design	Population	Intervention	Comparator	Primary Outcome	Results
Double-blind, crossover RCT	Adults with cancer-related depression and anxiety N = 12	0.2 mg/kg psilocybin Psychotherapy	Niacin (placebo) Psychotherapy	Blood pressure and heart rate measurements at baseline and during session BDI at baseline, 1 day, 2 weeks, and months 1, 2, 3, 4, 5, and 6	Statistically significant elevations in blood pressure and heart rate, but not considered clinically significant Mean BDI change from 16.1 at baseline to 10.0 at 2 weeks was not sustained or statistically significant

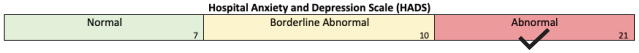
- Study was conducted to assess the feasibility and safety of moderate doses of psilocybin
- Participants wore Holter monitors throughout sessions with no reports of dysrhythmias or conduction disturbances

Grob CS, Danforth AL, Chopra GS, et al. Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Arch Gen Psychiatry*. 2011;68(1):71-78. doi:10.1001/archgenpsychiatry.2010.116

Ross, et al. 2016

Design	Population	Intervention	Comparator	Primary Outcome	Results
Double-blind, crossover RCT	Adults with cancer-related depression and anxiety N = 29	0.3 mg/kg psilocybin Psychotherapy	Niacin 250 mg (placebo) Psychotherapy	Investigator-defined clinically significant response: 50% reduction in HADS, BDI, others	**At 7 weeks:** 81% of patients in psilocybin-first group met criteria for the primary outcome, versus 14% of patients in the niacin (placebo) group

- Niacin thought to serve as a better control due to flushing reaction
- Pre-treatment and post-treatment therapy support was not standardized among participants
- Statistically significant response rates were not sustained at 26 weeks
- MEQ-30 scores were associated with clinical benefit in 7-week therapeutic assessments



Ross S, Bossis A, Guss J, 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):1165-1180. doi:10.1177/0269881116675512

Griffiths, et al. 2016 (1) – Study Design

Design	Population	Intervention	Comparator
Double-blind, crossover RCT	Age 21-80 with cancer-related depression and anxiety N = 51	22-30 mg (0.3-0.4 mg/kg) psilocybin Psychotherapy	1-3 mg psilocybin (placebo) Psychotherapy

- Assessments taken five weeks after each session; then groups crossed over

Griffiths RR, Johnson MW, Carducci MA, 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):1181-1197. doi:10.1177/0269881116675513.

Griffiths, et al. 2016 (2) – Results

Outcome	Group	Baseline	Post-Session 1 (5 weeks post)	Post-Session 2 (5 weeks post)	6 months
GRID-HAMD-17	Low-dose first	22.32 (0.88)	14.80 (1.45) p = < 0.05	6.50 (0.86) p = < 0.001	6.95 (1.24) p = < 0.001
	High-dose first	22.84 (0.97)	6.64 (1.04) p = < 0.001	6.52 (1.44) p = > 0.05	6.23 (1.30) p = < 0.001
HAM-A	Low-dose first	25.68 (0.89)	16.64 (1.53) p = < 0.05	8.92 (1.14) p = < 0.001	7.95 (1.19) p = < 0.001
	High-dose first	25.73 (1.11)	8.48 (1.16) p = < 0.001	7.52 (1.27) p = > 0.05	7.04 (1.17) p = < 0.001

*Numerical data reflect the means with (standard error of the mean)

Griffiths, et al. 2016 (3) – Results Discussion

- Included 17 diverse therapeutic outcome measures in the primary outcome
- MEQ-30 scores correlated with outcome measures at five weeks following high-dose psilocybin sessions
- The reduction of scores on multiple scales strengthens the association of psilocybin use and benefit

What About Microdosing?

- Clinical trials have assessed outcomes related to productivity, creativity, and other similar measures
- Microdosing has not been evaluated in the treatment of depressive disorders
- **Challenges:**
  - Set and setting
  - Tolerance

Literature Recap

- High heterogeneity in methodology between studies
- Most studies had small sample sizes and short follow-up periods
- Adequate blinding is challenging in clinical trials
- Psilocybin achieved defined clinical response in the vast majority of modern studies

Clinical Trials Discussion

Available Guidance for Clinical Trials

Guidelines for human hallucinogenic research published by researchers at Johns Hopkins University (Johnson, et al 2008)

Recommendations for:

Selection of study participants and personnel	The environment of psilocybin-assisted sessions	Preparation of study participants	Best practices for hallucinogen administration

Ethical and Legal Considerations

- No consensus for the minimum qualifications required to oversee psilocybin-assisted therapy
- Offering widespread, accessible psychedelic therapy will need to be balanced with effective psychotherapeutic support
- Concern for personal use of psychedelics amongst researchers and implications for introducing bias and public perception
- Must ensure appropriate controlled substance scheduling between agents

The Role of Psychotherapy

- 39% of survey respondents stated taking psilocybin was one of the five most challenging experiences of their lifetime
  - 62% reported the experience to be in the top ten most meaningful experiences in their lifetime
- An association between the subjective psychedelic response and clinical benefit has been observed in clinical trials
- Mitigation of risk associated with psychedelic use

Conclusion

Image: Montoyo, A. "Hallucination." *Flickr*, 3 Dec 2018, https://www.flickr.com/photos/139341301@N08/44358826880/in/gallery-197474421@N06-72157721429247032/

Summary

- Clinicians will see more widespread therapeutic and illicit use of psilocybin
- Psilocybin is a promising novel therapy for depression, but clinical trials have significant limitations
- Standard practice for psychotherapy has not been established, yet has an essential role in psilocybin treatment
- Natural Medicines™ is a helpful resource to look to first for questions that arise, and there is new literature published every day

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