

Psilocybin: *4-phosphoryloxy-N,N-dimethyltryptamine*

# ARIZONA

## Poison and Drug Information Center



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# Psilocybin and human history;

- Algerian rock art and South American artwork describe human interaction with mushrooms



FIGURE 3. The bee-faced mushroom shaman of Tassili-n-Ajjer. Drawing by Kathleen McKenna. From O. T. Oss and O. N. Oeric, *Psilocybin: The Magic Mushroom Grower's Guide*, 1986, p. 71. From the original in Jean-Dominique Ajoux, *The Rock Paintings of the Tassili* (New York: World Publishing, 1963), 71.



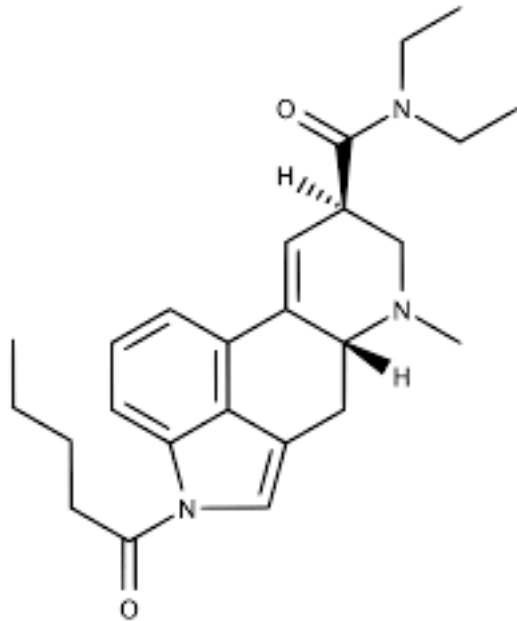
Various Mushroom Stones (types 18 to 21) - 8000 B.C. to 500 A.D.)

Akers, BP, Ruiz, JF, Piper, A, Ruck, CAP. A prehistoric mural in Spain depicting neurotropic psilocybe mushrooms? *Econ Bot.* 2011;65(2):121-128. doi:10.1007/s12231-011-9152-5.

# Use of psilocybin:

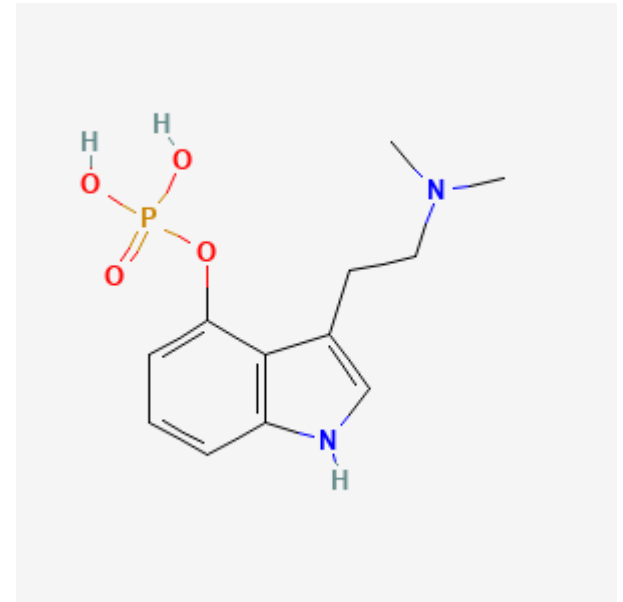
- a survey published in 2021 of more than 7,000 people, some 7%—or about 500 people—reported having used psilocybin mushrooms in the past year.

LSD

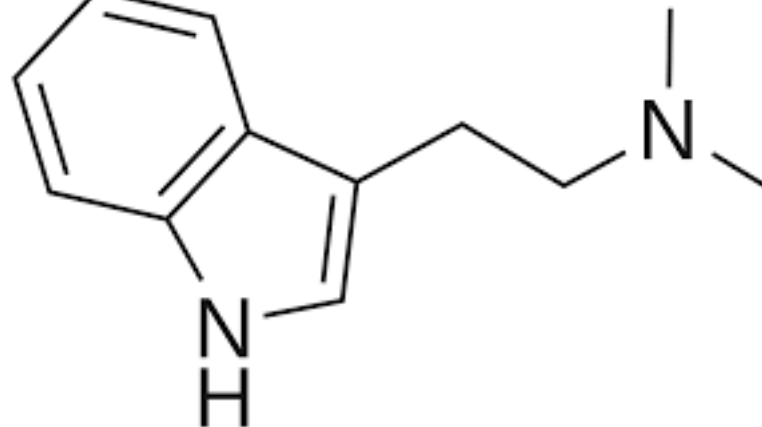


Structure:

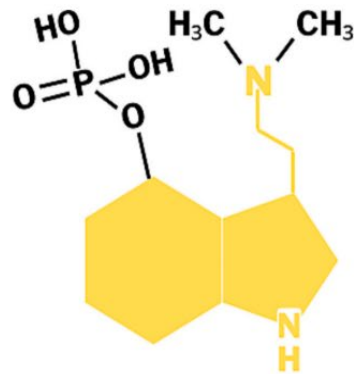
Psilocybin



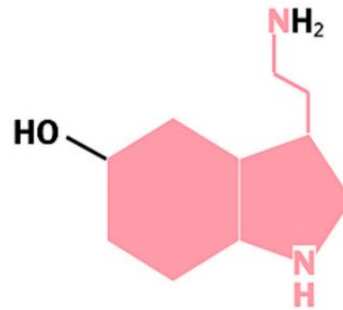
DMT



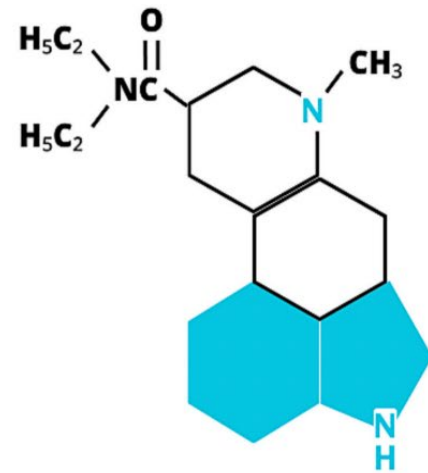
# Structural core of psychedelics:



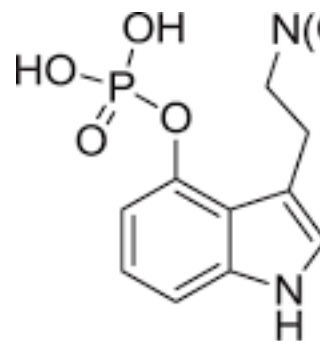
Psilocybin



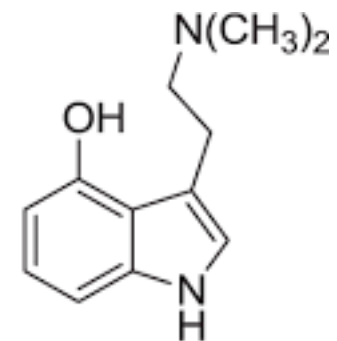
Serotonin



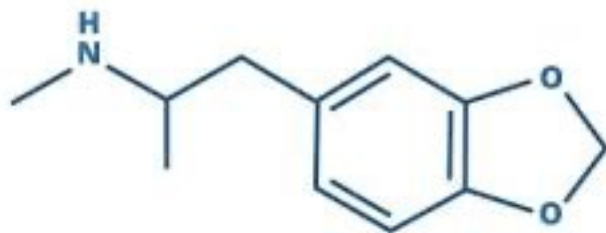
LSD



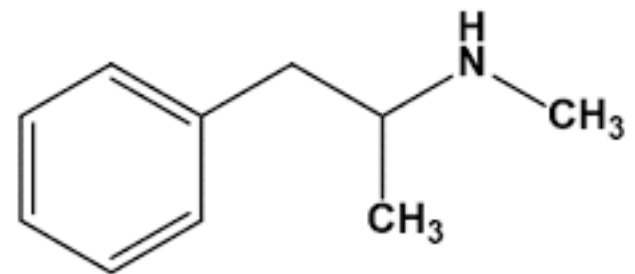
Psilocybin



Psilocin



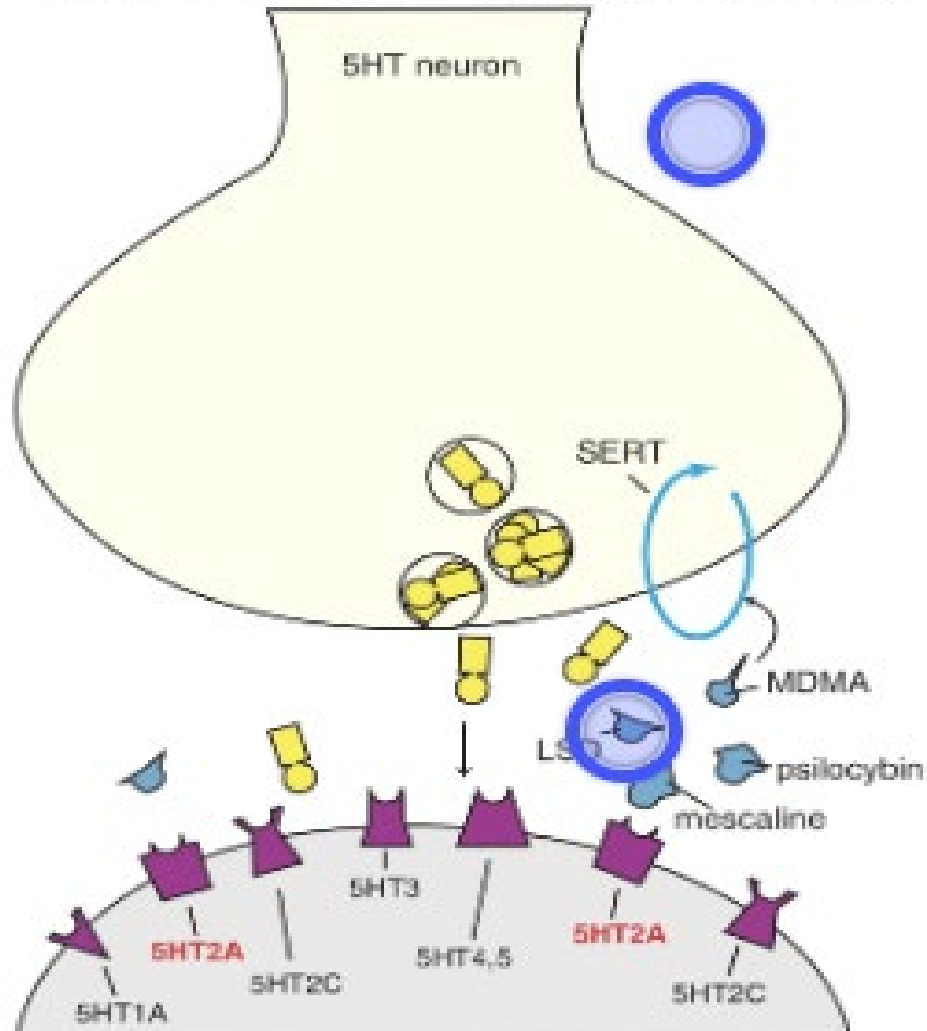
MDMA (3,4-methylenedioxyamphetamine)



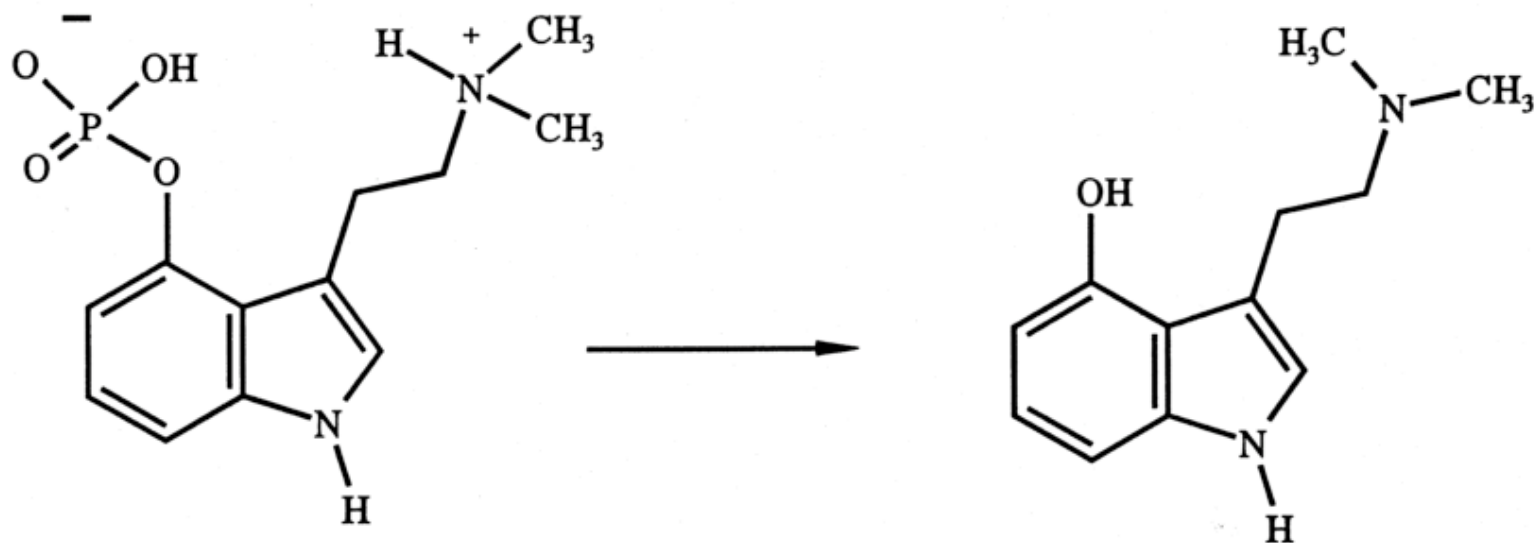
(C<sub>10</sub>H<sub>15</sub>N; molecular weight = 149.24)

# Interaction with receptors:

Mechanism of Hallucinogens at 5HT2A receptors



## Metabolism to the active compound



Psilocybin

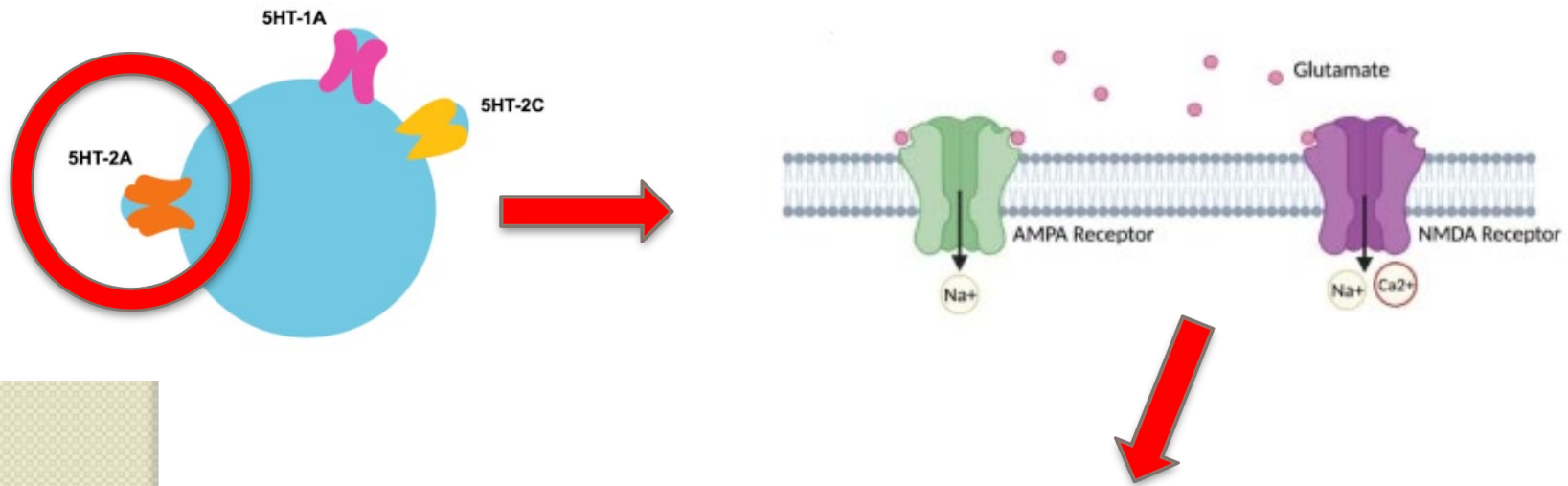
Psilocin



# The main receptor of Psilocin:

## Psilocybin

### Mechanism of Action

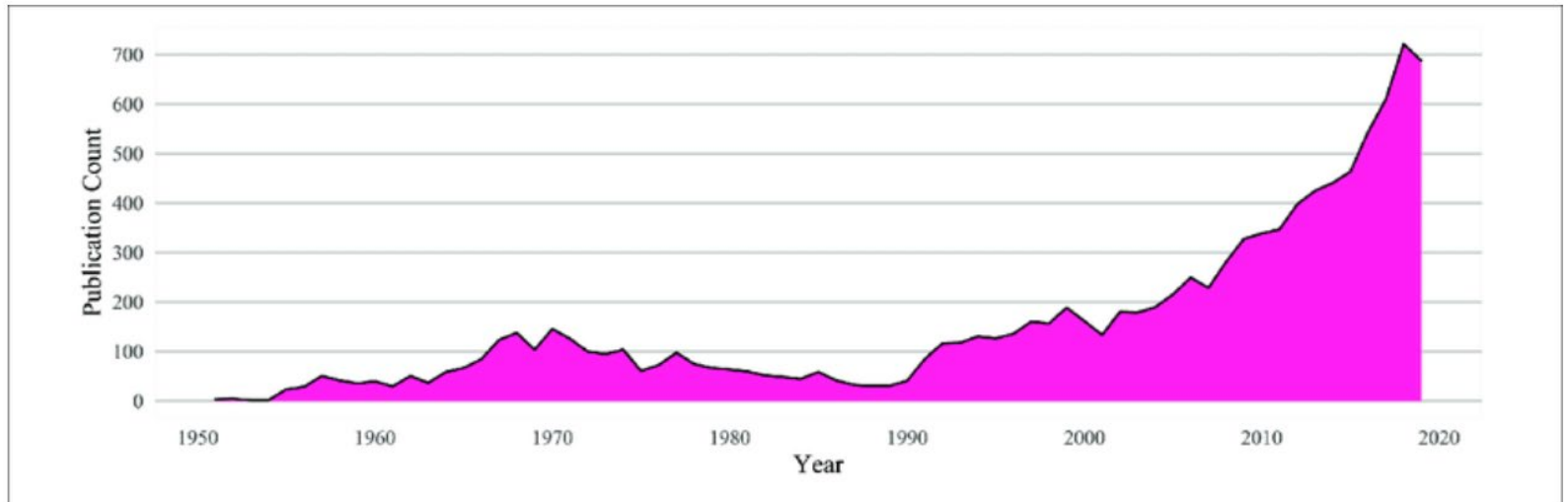


Increase Dopaminergic activity in the ventral Striatum of the brain  
And decrease IL-6 and TNF-alpha

# Modern History Psilocybin:

- 1957 Isolated by Albert Hofmann.
- 1958 Synthesized.
- 1970 Controlled Substance Act.
- 1992 NIDA and FDA opens research into psychedelics

# Resurgence of Psychedelics:



Web of science psychedelic publication count by year.

# Proposed Psychedelic-assisted therapy:

- Substance USE disorders
- Depression
- Anxiety
- Obsessive-compulsive disorder
- PTSD

# Dose, onset, duration of effects:

- Dose: 40mcg/Kg
- Onset: 20-40 minutes.
- Duration: 3-6 hours

•[Journal List Ment Health Clin v.7\(1\); 2017 Jan PMC6007659](#)

August 31, 2023

# Single-Dose Psilocybin Treatment for Major Depressive Disorder

## A Randomized Clinical Trial

Charles L. Raison, MD<sup>1</sup>; Gerard Sanacora, MD, PhD<sup>2</sup>; Joshua Woolley, MD, PhD<sup>3,4</sup>; [et al](#)

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*JAMA*. 2023;330(9):843-853. doi:10.1001/jama.2023.14530



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# Trial of Psilocybin versus Escitalopram for Depression

**Authors:** Robin Carhart-Harris, Ph.D., Bruna Giribaldi, B.Sc., Rosalind Watts, D.Clin.Psy., Michelle Baker-Jones, B.A., Ashleigh Murphy-Beiner, M.Sc., Roberta Murphy, M.D., Jonny Martell, M.D., Allan Blemings, M.Sc., David Erritzoe, M.D., and David J. Nutt, M.D. [Author Info & Affiliations](#)

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[Heliyon](#). 2022 Dec; 8(12): e12135.

PMCID: PMC9758406

Published online 2022 Dec 6. doi: [10.1016/j.heliyon.2022.e12135](https://doi.org/10.1016/j.heliyon.2022.e12135)

PMID: [36536916](https://pubmed.ncbi.nlm.nih.gov/36536916/)

## Single-dose psilocybin for treatment-resistant obsessive-compulsive disorder: A case report

[Benjamin Kelmendi](#),<sup>a,b,1,\*</sup> [Stephen A. Kichuk](#),<sup>a,1</sup> [Giuliana DePalmer](#),<sup>a</sup> [Gayle Maloney](#),<sup>c</sup> [Terence H.W. Ching](#),<sup>a</sup> [Alexander Belser](#),<sup>d</sup> and [Christopher Pittenger](#)<sup>a,d,e,f</sup>

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# Clinical trials:

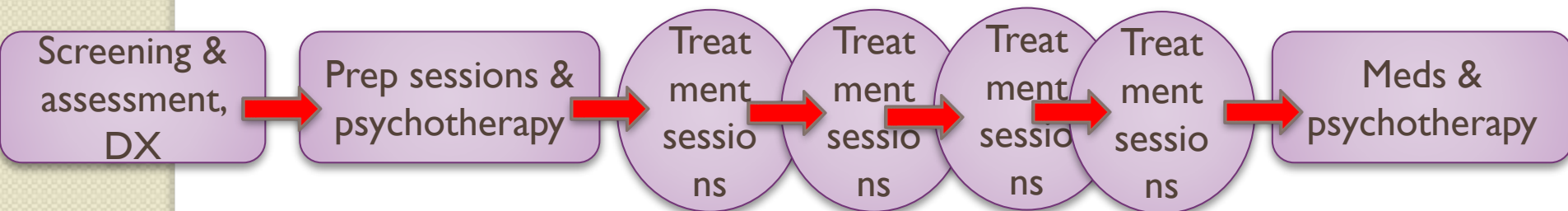
## Clinical Trials Involving Psychedelics Published During the Present 'Second Wave' of Psychedelic Research

Study	Population/indication and sample size	Drug and design	Main efficacy outcome
<a href="#">Moreno et al (2006)</a>	Obsessive compulsive disorder, n=9	Psilocybin: single-arm, within subjects, variable doses. Up to four doses of psilocybin	All patients showed improvements within 24 h of a treatment but no effect of dose
<a href="#">Grob et al (2011)</a>	Anxiety and depression in end-stage cancer, n=12	Psilocybin: DB-RCT, crossover, inert placebo. Single dose of psilocybin	Significant reductions in trait anxiety at 3 months and depression at 6 months
<a href="#">Johnson et al (2014)</a>	Long-term chronic tobacco smoking, n=15	Psilocybin: open-label. Up to three doses of psilocybin after four CBT sessions	80% of sample abstinent at 6 month follow-up
<a href="#">Gasser et al (2014)</a>	Anxiety related to life-threatening disease, n=12	LSD: DB-RCT, crossover, very low dose (VLD) LSD=control. Single dose of LSD	Significant decreases in state and trait anxiety vs VLD at 2 months and sustained for 12 months
<a href="#">Bogenschutz et al (2015)</a>	Alcohol dependence, n=10	Psilocybin: open-label. Up to two doses after seven motivational therapy sessions	Significant decrease in drinking behaviors for up to 9 months
<a href="#">Osorio Fde et al (2015)</a> and <a href="#">Sanches et al (2016)</a>	Major depressive disorder (MDD), n=6+study extension to n=17	Ayahuasca: open-label. Single dose of ayahuasca	Significant decreases in depressive symptoms for up to 21 days
<a href="#">Carhart-Harris et al (2016a, b)</a>	Treatment-resistant MDD, n=12+study extension to n=20	Psilocybin: open-label. Two doses of psilocybin	Significant decreases in depressive symptoms for up to 6 months
<a href="#">Ross et al (2016)</a>	Anxiety and depression related to life-threatening cancer, n=29	Psilocybin: DB-RCT, crossover, niacin=active placebo. Single dose of psilocybin	Significant decreases in anxiety and depression vs niacin at 7 weeks (pre crossover) and sustained for 6.5 months
<a href="#">Griffiths et al (2016)</a>	Anxiety and depression related to life-threatening cancer, n=51	Psilocybin: DB-RCT, crossover, VLD psilocybin=control. Single dose of psilocybin	Significant decreases in anxiety and depression vs VLD at 5 weeks (pre crossover). Effects sustained for 6 months

Abbreviations: DB-RCT, double-blind randomised controlled trial; VLD, very low dose; MDD, major depressive disorder; TRD, treatment-resistant depression.

# Common aspects of therapy:

- Screening & Diagnosis.
- Preparatory sessions & psychotherapy.
- Multiple treatment sessions over weeks.
- Maintenance: conventional medication and psychotherapy.







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