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A lexicon for psychedelic research and treatment

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Abstract

Psychedelics are undergoing a clinical research renaissance, with compounds such as psilocybin advancing to Phase 3 trials for treatment-resistant depression and receiving fast-track or breakthrough designations from regulatory agencies. Despite this progress, the field lacks standardized terminology to guide clinical development, dosing, safety monitoring, and regulatory classification. Here, we present a comprehensive framework for psychedelic nomenclature based on pharmacology, subjective effects, dosing, and therapeutic use. A pharmacological classification system is described, encompassing serotonergic, glutamatergic, kappaergic, GABAergic, and atypical psychedelics. Dose-dependent categories—microdose, minidose, mididose, and macrodose—are introduced to standardize the description of dosing levels and intended subjective effects. We also standardize vague terms like "short-acting" or "long-acting" with specific pharmacokinetic parameters, including route, onset, and duration of action. Safety considerations are also explored, particularly cardiovascular and psychological effects, and we discuss the need for risk mitigation protocols in higher-risk compounds like ibogaine. The evolving role of psychotherapy in psychedelic treatment is also examined, proposing terminology to distinguish between "psychedelic therapy" and varying levels of psychological support. A three-phase treatment model—preparation, dosing, and integration—is recommended as a minimum standard for safe and effective care. The lack of comparative research on psychotherapy modalities in psychedelic therapy is identified as a critical gap. Ultimately, a standardized lexicon and clinical framework will support clearer communication, improved trial design, and more equitable access as psychedelic therapies move toward widespread clinical use.

Keywords

psychedelics, psychedelic-assisted therapy, microdose, psychoplastogen, macrodose

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Introduction

Psychedelic drugs such as psilocybin, LSD, DMT, 5-MEO-DMT, and ibogaine are becoming widely researched for clinical utility with psilocybin currently in a Phase 3 trial for treatment-resistant depression under the food and drug administration fast track process. Despite this advancement, there is little discussion about the appropriate terminologies to use for these drugs. Changes to medical dictionary for regulatory activities coding terms are needed for collecting critical safety end points for psychedelics during clinical development. The duration of psychedelic effects creates further confusion especially in relation to describing drug products as short-acting versus long-acting psychedelics. Also, microdosing of psychedelics which result in low plasma concentrations raise the need for comparator terminology for distinguishing placebo effects as these are frequently used as an active comparator group in clinical trials. This article attempts to provide a theoretical framework for a psychedelic lexicon that clarifies terms and definitions to facilitate future pharmaceutical research and clinical use.

What to call these drugs?

Traditionally under international pharmacology conventions (e.g., World Health Organisation (WHO) (2025), psychedelics have been interchangeably called hallucinogens. We believe "hallucinogen" to be a pejorative term that was developed and used in part to justify the banning of these substances under the 1971 United Nations Convention on Narcotic Drugs (Nutt et al., 2013). The term "hallucinogen" implies the production of significant mental abnormalities, associating these drugs with the production of pathological brain states like those seen in illnesses such as schizophrenia and manic delirium. De facto, this connotation has the effect of alarming possible prescribers, propagating stigma around the safety of these compounds, and undermines belief in therapeutic effects.

Psychedelic (from the Greek mind-manifesting) is a term that has come into general use over the past decades by those working in the field. There is a general consensus that it should be used, especially when the doses of the drugs given produce profound alterations in consciousness. Psycholytic doses describe the administration of doses that are perceptual and involve some active psychotherapy while acutely under the drug. When they are used at subpsychedelic doses, this should be specified and the actual doses and the subjective/mechanistic effects targeted should be reported—see the Dosing section below.

Drugs developed from the same chemical scaffolds as psychedelics, for example, selective 5-HT2A/1A agonists but without psychedelic effects, though with possible antidepressant and neuroplastic activity, are a topic of great innovation at present (Cao et al., 2022). Currently, the evidence for a lack of psychedelic effect is based on head twitch response in rodent behavioral studies and anatomical evidence of neurite outgrowth. Psychedelics are theorized to produce lasting durability of effects because they open a period of increased neuroplasticity, potentially leading to changes in brain structure and function. If this mechanism of action is confirmed in human studies, then psychedelics will be classified under a new drug category as psychoplastogens or neuroplastogens (Nardou et al., 2023; Olson, 2018).

Pharmacological classification (Table 1)

This approach is one based on pharmacological activity as by the neuroscience-based nomenclature expert group (Zohar et al., 2015). Here, the primary discriminator is the pharmacological target for the drugs. For "classical" or serotonergic psychedelics such as psilocybin, lysergic acid diethylamide (LSD) and N,N-dimethyltryptamine (DMT), their effects are mediated via the 5-hydroxytryptamine 2A (5-HT2A) receptor where they act as agonists or partial agonists. This evidence is provided by biochemical assays and confirmed by the blockade of psychedelic experiences by 5-HT2A receptor antagonists, for example, ketanserin, risperidone, and mirtazapine (Holze et al., 2024). Affinity at the 5-HT2A receptor is correlated with potency among different psychedelics (Glennon et al., 1984), and for psilocybin, brain 5-HT2A receptor occupancy predicts the intensity of subjective effects (Madsen et al., 2019). Thus, we suggest these drugs are called serotonergic psychedelics.

Other drugs or natural products can have psychoactive effects that are also described as "psychedelic like." These include muscimol (from *Amanita muscaria*), ketamine, and salvinorin A (from *Salvia divinorum*) that act on other neurotransmitter receptors (see Table 1).

We suggest ketamine and related dissociative anesthetics, for example, PCP are called glutamatergic psychedelics, salvinorin A be called a kappaergic psychedelic (Chavkin et al., 2004), muscimol a GABAergic psychedelic (Rivera-Illanes and Recabarren Gajardo, 2024), and ibogaine an atypical psychedelic (Mash, 2023).

Dosing levels—Table 2

Unlike most other drugs or medicines approved for therapeutic use, psychedelics are used in a wide range of doses, even at doses that are subjectively undetectable (very low dose range in what is currently labelled as "microdosing"). Table 2 contains a suggested nomenclature with estimated dose levels to produce subpsychedelic effects in humans. A macrodose produces a psychedelic effect. A mididose produces noticeable subjective alterations such as change in sensory perception but without frank distortions and/or peak psychological or mystical-type experiences. This level of effect is what historically has been called a "psycholytic"

Table 1. Pharmacology of psychedelics.

Suggested term	Drug class or source	Common chemical compounds	Pharmacology	Antagonists
Serotonergic psychedelics	Fungi (e.g., magic mushroom) Plants (e.g., San Pedro cacti) Reptiles (e.g., Sonora toad)	LSD, psilocybin, DMT, mescaline, and 5-MEO-DMT[a]	5-HT2A receptor agonists	Ketanserin Risperidone Olanzapine Mirtazapine
GABAergic psychedelics	*Amanita Muscaris*	Muscimol	GABA-A receptor agonist	Bicuculline[b] Gabazine[b]
Kappaergic psychedelics	*Salvia divinorum*	Salvinorin-A	Kappa-opioid receptor agonist	Naltrexone Buprenorphine
Glutamatergic psychedelics		Phencyclidine Ketamine	NMDA glutamate receptor antagonists	N/A
Atypical or mixed	*Iboga*	Ibogaine Noribogaine	NMDA glutamate receptor antagonist and Kappa opioid receptor agonist	Unknown

[a]Note re 5-MEO-DMT—the functional pharmacology of this molecule in humans is still uncertain as blocking studies with 5-HT2A (or other receptor) antagonists have not yet been done. Whilst it has very much higher affinity for the 5-HT1A receptor than 5-HT2A subtype many (though likely not all) of its effects appear mediated through 5-HT2A receptor agonism (Riga et al., 2014). LSD: Lysergic acid diethylaminde; DMT: N,N dimethyltryptamine 5-MEO-5-methoxy; GABA-A: Gamma-amino-butyric acid; NMDA: N-methyl D-aspartate; N/A: not applicable.
[b]Not proven in humans.

Table 2. Suggested dosing terminology and amounts.

Drug	Macrodose	Mididose	Minidose	Microdose
Psilocybin	25–30 mg	10 mg	5 mg	1 mg
LSD	100–150 µg	50 µg	20 µg	< 12 µg
DMT	15–20 mg i.v.	N/A	N/A	N/A
5-MeO-DMT	10–12 mg i.v./nasal	N/A	N/A	N/A
Mescaline	>500 mg	250 mg	50–100 mg	25 mg
Ketamine	>0.7 mg/kg i.v./i.m.	N/A	N/A	N/A
Muscimol	>15 mg	5–10 mg	1 mg	<1 mg
Salvinorin-A	200–500 ug	?	?	N/A
Ibogaine	600–800 mg	300 mg	100 mg	<20 mg

Note. All oral unless specified. N/A = not applicable.

dose and was widely used to facilitate psychotherapy in the 1950s and 1960s particularly with LSD (Passie et al., 2022). For reasons of patient preference (they declined the option of a macrodose), this approach has recently been used in a treatment trail of OCD. A 10-mg psilocybin dose was compared with a 1 mg (placebo) dose and found to have significant clinical benefits (Pellegrini et al., 2025).

A minidose produces just detectable subjective effects (Madsen et al., 2019). At Imperial College, we are conducting a trial of a 5 mg dose of psilocybin in young people who self-harm to explore if this minidose might facilitate cognitive retraining of more adaptive behaviours in response to stressors. It is plausible that such a minidose might promote cognitive flexibility and possibly have neuroplastic effects.

By definition, a microdose has no detectable effects (Szigeti et al., 2024). However, it is plausible that such low doses might have brain effects such as neuroplasticity, particularly if taken over a long period. In unregulated practice, many people who are self-microdosing take doses that they can just perceive an effect of: they are minidosing. Such doses can produce slight but measurable subjective and physiological effects compared with placebo (Murphy et al., 2023). Where true microdoses are used, then the effects are generally indistinguishable from placebo (Szigeti et al., 2021).

Dosing levels as in Table 2 are just an estimate as effects can vary for several reasons such as individual metabolism, sensitivity to subjective effects and the impact of other medicines. A good example of this comes from the recent Compass Pathways trial, where a 10-mg psilocybin dose produced significant psychedelic experiences in a proportion of patients that were equivalent to those produced by

Table 3. Kinetics by route of administration.

Drug	Route	Time to max effect	Duration of subjective effect
DMT	Smoked/i.v. bolus	1–2 min	20 min
DMT	Oral (ayahuasca)	1–2 h	4–6 h
DMT	i.v. bolus	5 min	10–20 min
LSD	Oral	1–2 h	10–14 h
	i.v. bolus	1–2 h	10–14 h
Psilocybin	Oral	1 h	4–6 h
	i.v.	5 min	1 h
5-MEO-DMT	Vaporized/intranasal	1–2 min	15–20 min
S. divinorum	Smoked	2–5 min	10–15 min
Amanita muscaria	Oral	30 min	3–6 h
Ketamine	Oral	1 h	3–4 h
	i.v. bolus	5–10 min	2–3 h
	Intranasal (esketamine)	10–20 min	30–90 min
Ibogaine/nor-ibogaine	Oral	1–2 h[a]	18–24 h[a]

LSD: Lysergic acid diethylamide; DMT: N,N-dimethyltryptamine 5-MEO 5-methoxy.
[a]Genotype-dependent cytochrome P450 metabolism (e.g., fast, slow or intermediate).

the 25-mg macrodose. Moreover, these psychedelic experiences were predictive of good clinical outcomes (Goodwin et al., 2025). The implication of these findings is that the intention of and subjective experiences from the specific dose used should be specified as part of the protocol and reporting.

Pharmacokinetics—Table 3

This term refers the onset and offsets time of psychedelics or pharmacodynamic effects. These parameters vary according to the drug, the formulation, and the route of administration. A shorthand has developed that refers to some serotonergic psychedelics (DMT and 5-MEO-DMT) as short acting and others (LSD and psilocybin) as long acting. This terminology can be misleading: for example, DMT when vaporized/inhaled or given i.v. as a bolus has a fast onset and short duration of action, but it can be infused i.v. to give a rapid onset but a long duration of action up to hours (Luan et al., 2024). And when DMT is taken orally in ayahuasca brew, it has a slow onset and a long duration of action of many (1–3) hours (Riba et al., 2001). Psilocybin taken orally builds up to a maximum effect over an hour and lasts for 4–6 h. But when given i.v., its effects are almost immediate and last less than an hour (Carhart-Harris et al., 2012). For these reasons, we suggest eliminating the use of terms such as short acting and replacing them with specific details of route and duration of activity and type of administration (and in the case of intravenous use either bolus or infusion; Table 3).

Non-medical use

Traditionally, non-medical use has been called recreational use. However, recreational use is often used in a pejorative way to imply rewarding hedonic misuse without a deeper purpose. Survey data suggest that a large proportion of non-medical users of psychedelic take them infrequently with a desire to explore the psychedelic experience and gain insights into the nature of consciousness (Kruger et al., 2025). We suggest this type of consciousness-exploratory use could be called experiential, naturalistic, or just non-medical use (though for some people this use may be as a form of self-medication; Kruger et al., 2025; Nygart et al., 2022). For centuries, Indigenous communities around the globe have used psychedelics as part of their contemplative social practices embedded in their traditional knowledge system (Urrutia et al., 2023).

Most serotonergic psychedelics can increase heart rate and/or blood pressure short-term to some extent, either directly on the cardiovascular system or indirectly, because of their psychological effects (Nahlawi et al., 2025). For most serotonergic psychedelics, the cardiovascular changes are not clinically relevant; rather, they are equivalent to the effect of climbing a set of stairs. In open label and clinical trial studies, these can be recorded using standard telemetry devices. If the vital signs (heart rate and blood pressure) are outside the normal range, they are clinically relevant and reported as adverse effects. Of course, people at higher risk due to hypertension and/or cardiac issues would need careful prescreening and close monitoring. Drug-related cardiac arrhythmias are considered low risk for this class of psychedelics.

Ibogaine is especially problematic due to its transient dose-related prolongation of the cardiac QTc interval (Glue et al 2016; Knuijver et al., 2022; Luz and Mash, 2022). Reports of drug-related deaths and other safety concerns associated with ibogaine administrations often occur due to impure drug product, massive overdoses, and the lack of medical monitoring of patients who are underdoing detoxification from drugs and alcohol in unsafe settings (Luz and Mash, 2021). Based on the known risk of QT prolongation of the drug, ibogaine treatment must be administered by knowledgeable physicians using risk mitigation protocols and real-time cardiac monitoring (Luz and Mash, 2021; Mash, 2023).

The psychological effects of psychedelics are usually profound, and for some people, especially those with a diagnosis of post traumatic stress disorder (PTSD) or treatment-resistant depression, can be distressing if historic traumas or fears are uncovered. When occurring with non-medical users, these challenging experiences are commonly referred to as "bad trips" and are considered an unwanted adverse effect of using the drugs. In the setting of clinical trials, unrepressed trauma may be of great therapeutic value in allowing participants access to, and recovery from, repressed memories. This effect of the drug is part of the therapeutic process in the same way as anxiety and fear are an inevitable element of exposure therapy for specific phobias or PTSD. Therefore, they should not be considered adverse effects and should not be reported as such in clinical trials unless they persist for a significant time, for example, several weeks, after the treatment period.

Emerging data—for example, from the Imperial College research team—have shown that in two psilocybin depression trials the subjective experience is predictive of outcome—with more mystical insights, ego dissolution, and emotional breakthrough predicting better clinical response (Roseman et al., 2018; Weiss et al., 2024). Expectation of positive outcome, however, did not predict the efficacy of psilocybin (Szigeti et al., 2024).

Psychotherapy and psychological support

It is important to define the roles and credentials of clinical staff who contribute to the patients' journey. As clinical trials advance and regulatory agencies weigh in on best practices, these positions will likely change over time. Today, several terms have been used, including, trip guides, sitters, and therapists. These roles carry significant clinical responsibility to properly prepare, support, and integrate the patients experience albeit their training, certification, and licensure vary widely across drug and treatment settings. A psychedelic therapist might be the best term, as is the case with MDMA where (if two people are present) the licensed clinician takes the clinical lead. We propose that "dosing assistant" should be used in lieu of "monitor" or "sitter" to refer to non-mental health professionals assisting with dosing sessions.

It is also important to disentangle the wide variety of terms that have been generated to represent psychedelic-related treatments, including psychedelic therapy, psychedelic-assisted therapy, psychedelic-assisted psychotherapy, and psychedelics with psychological support. In brief, we believe these terms all fall under the umbrella of "psychedelic therapy" with each term representing differing levels of interpersonal support. "Psychedelic-assisted therapy" and "psychedelic-assisted psychotherapy" are generally used interchangeably in the literature, but conceivably "psychedelic-assisted therapy" could involve associating psychedelics with treatments that are not considered "psychotherapy" (e.g., physical therapy).

Regarding psychedelics with psychological support, there is debate among the field whether the psychological support administered in trials should be considered psychotherapy. The American Psychological Association defines psychotherapy as "any psychological service provided by a trained professional that primarily uses forms of communication and interaction to assess, diagnose, and treat dysfunctional emotional reactions, ways of thinking, and behaviour patterns" (APA, 2024). Given this definition, the psychological support administered in most psychedelic trials would be considered psychotherapy (Aday et al., 2024). Nonetheless, psychedelics with psychological support have generally been used to characterize psychedelic dosing that does not include preparation or integration psychotherapy, although a psychotherapist may be present during the dosing session to enhance safety.

Minimum treatment set

The re-emergence of psychedelic therapy over the past two decades has largely been done according to a three-phase program: preparation sessions, a treatment session, and then one or often several integration sessions (Watts et al., 2017; Aday et al., 2022). Where possible, these are typically given over three consecutive days by the same people. This is typically what is meant by the term "psychological support" that is referred to in most of the published and ongoing research.

The rationale here is to educate and prepare participants (either patients or healthy volunteers for first in human studies) for the unique and profound psychological effects of psychedelics. This preparation is designed to minimize anxiety which thought to be a predictor of poor clinical outcomes (Roseman et al., 2018). It also thought to help participants maximize the benefits of their psychedelic experience especially by encouraging them not to try to control or resist the experience, which can reduce its strength and value but to go with it to explore their inner self—an often used catch line is "in and through" or "go with the flow" of their personal inner journey.

There is little research on alternative approaches probably because it seems unlikely that ethics committees, on safety grounds, would approve studies without these elements. Moreover, patients and healthy volunteers find them reassuring and valuable, and they likely add to safe outcomes and therapeutic value (Schenberg et al., 2024).

The area of significant contention is whether more intensive psychotherapeutic sessions add value and if so what modalities (integrative, cognitive behavioral, etc.) of psychotherapy are best suited to a given psychedelic therapeutic? There is little to no systemic research on this topic in the treatment of depression with serotonergic psychedelics. Currently, there are no comparative studies of different forms of psychotherapy in combination with serotonergic psychedelics.

The situation with ketamine is rather different. Initially, ketamine treatment—either with racemic ketamine or with esketamine—was given without therapy, a procedure colloquially called "liquid ECT." However, this approach might have led to ketamine not performing as well as it could: one recent trial of ketamine in alcohol addiction that showed that ketamine + mindfulness-based psychotherapy performed better than ketamine + education Moreover just three ketamine sessions produced enduring reductions in drinking behavior (Grabski et al., 2022). This approach has been developed as a manualized treatment regime with three ketamine sessions that is now the subject of a major phase 3 UK trial funded by the NIHR (https://sites.exeter.ac.uk/morekare). Some health care providers in the United Kingdom now offer three to four ketamine + psychotherapy sessions for treatment-resistant depression and addictions, and some clinics that previously just used intravenous ketamine for depression are now beginning to offer psychotherapy interventions as well to explore if they add value. This is an important area for future research with both racemic ketamine and esketamine.

The most contentious issue at present in the use of psychedelics for mental illnesses is how many post-treatment psychotherapy sessions, other than one or two integration ones, should be offered. One extreme is to provide none, simply ask the patients to return to the care provider that they were under prior to the psychedelic treatment. The other extreme is to provide a full course of psychotherapy by the same therapist(s) who were present during the trip. This is of course significantly more expensive than the other approach and could make psychedelic therapy too pricey for some providers, even if it could be shown to deliver better outcomes.

An interesting hybrid model that some are exploring is to allow the prior/current therapist to be present in the psychedelic session(s). As well as being something patients sometimes ask for as it offers continuity of care with someone they know and trust, it can provide the prior therapist with insights to work on in future sessions. Such a study in gambling addiction is now underway at the Imperial College. This approach has the added value increase the number of therapists who have experience of psychedelic therapy, which is likely to be a limiting issue for the expansion of the field.

Patients' opinions are also important. We know that most patients who have had psilocybin therapy are very keen on having several psychotherapy follow-up sessions as many have lots of questions relating to the insights gained in the trip. When these are not available some have begun to set up their own self-help therapy/integration groups. It might be that shorter trips for example, those produced by a short (pulse) dose of DMT or 5-MEO-DMT do not produce so many questions and so less (or even no) therapy might be required. This is an area of urgent research need.

Conclusion

To date, there has been a lack of consensus in the field of psychedelic research regarding key terms. It is our hope that development of this lexicon can aid in translating findings across various research groups and improve clarity and precision in our communications with each other and the general public. We welcome your comments and feedback – please send them to d.nutt@imperial.ac.uk

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