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Patent Highlight

Targeting Phantom Pain with Psilocybin: Toward Integration with Adaptive Sensory Technologies

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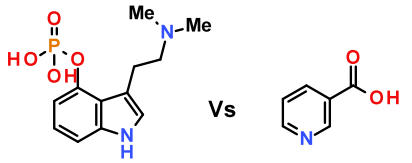
ABSTRACT: Psilocybin demonstrates a clinically meaningful reduction in phantom and residual limb pain. Adaptive sensory environments (ASEs) separately offer biosensor-guided modulation of psychological states during psychoactive therapy. This Patent Highlight explores the pharmacological findings of a psilocybin trial and discusses future integration with ASE systems to precision and scale psychedelic-assisted interventions.

Important Compound Classes.



Psilocybin
Phantom limb pain reduced by 58.9%

Niacin
Phantom limb pain reduced by 2.8%

Title. Psilocybin for Treating Phantom Pain; and Adaptive Sensory Environment Facilitating Psychoactive Therapies.

Patent Publication Number. WO 2025/038542 A1 (URL: https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2025038542&_cid=P22-M8S0UM-35749-1); WO 2024/263600 A2 (URL: https://patents.google.com/patent/WO2024263600A2/en?oq=WO+2024%2f263600+A2).

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Priority Date. August 11, 2025; June 20, 2023

Inventors. Geyer, M. Halberstadt, A.; Zeidan, F.; Furnish, T.; Castellanos, J.; Vieten, C. (WO 2025/038542 A1); Mann, S.; Gravelle, M.; Miller, N.; Manteau-Rao, M.; Lembcke, S. (WO 2024/263600 A2).

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Disease Area. Psychiatric disorder

Biological Target. 5-HT2A

Summary. Phantom limb pain (PLP) and residual limb pain remain difficult-to-treat neuropathic conditions following amputation. Central sensitization and maladaptive cortical representations contribute to their persistence. Emerging evidence suggests that serotonergic psychedelics like psilocybin may offer relief by inducing neuroplastic changes that reconfigure pathological sensory circuits.

Psilocybin for Phantom Pain. A recent placebo-controlled, double-blind trial reported in patent application WO 2025/038542 A1 evaluated the safety and efficacy of a single 25 mg oral dose of psilocybin in amputees with moderate to severe PLP. Participants receiving psilocybin showed a 58.9% reduction in PLP intensity at 2 weeks and a 79.9% reduction in residual limb pain, compared to minimal change or worsening in the placebo group. These effects persisted through 4 weeks post-treatment.

Mechanistically, psilocin—the active metabolite of psilocybin—acts as a 5-HT2A receptor agonist, modulating thalamocortical signaling and somatosensory network connectivity. Participants reported high perceived efficacy and did not experience any serious adverse events. The findings provide compelling evidence for psilocybin's central analgesic properties in neuropathic pain contexts.

The Role of Adaptive Sensory Environments. While the psilocybin study demonstrated pharmacologic efficacy in a tightly controlled clinical setting, the broader adoption of psychedelic therapy faces logistical challenges: high therapist burden, interindividual variability, and difficulty standardizing psychological support.

Patent application WO 2024/263600 A2 introduces an Adaptive Sensory Environment (ASE) system that could address these limitations. Although the researchers did not use the ASE in the psilocybin PLP trial, they designed it to

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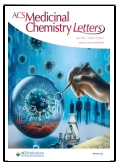


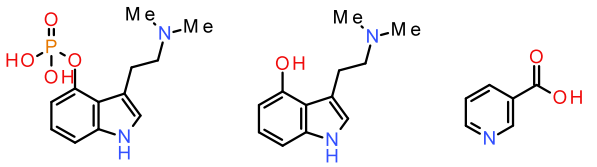
complement psychedelic therapy by enabling biosensor-driven monitoring and real-time adjustment of immersive XR (extended reality) environments. Biosensors track heart rate variability, EEG, electrodermal activity, and other physiological parameters to infer the user's emotional state. This enables automated modulation of sensory input (e.g., visual, auditory, tactile) to optimize therapeutic receptivity.

Toward Future Integration: A Speculative Synergy. Although no current studies have integrated ASE systems with psilocybin for pain, future protocols may benefit from combining pharmacologic intervention with context-sensitive sensory modulation. ASE could assist in predosing psychological preparation, guide arousal levels during altered states, and enhance integration post-treatment. Such integration may reduce the need for continuous human facilitation, improving scalability while preserving individualized care.

This remains speculative until validated by prospective trials, but the conceptual synergy—psychedelic pharmacodynamics aligned with real-time emotional conditioning—holds promise for transforming the delivery of psychedelic-assisted therapy.

As such, psilocybin shows durable and meaningful efficacy in phantom and residual limb pain. Future studies should explore how adaptive technologies like ASE might support the psychological dimensions of psychedelic therapy. The intersection of neuropharmacology and digital biosensing represents a promising frontier in pain medicine and mental health.

Key Structures.



Biological Assay. Clinical pain assessments included the Visual Analog Scale (VAS) for phantom and residual limb pain intensity and the Brief Pain Inventory (BPI) for pain severity and interference with daily function. Safety evaluations comprised the Columbia-Suicide Severity Rating Scale (C-SSRS), vital sign monitoring (blood pressure and heart rate), and the Monitor Rating Questionnaire for acute adverse effects (e.g., anxiety, nausea). Subjective experiences were assessed using the Five-Dimensional Altered States of Consciousness (5D-ASC) scale and effectiveness ratings at 2- and 4-week follow-ups. Exploratory rationale included fMRI data highlighting changes in the somatosensory cortex and default mode network (DMN).

Biological Data. The table presents the mean pain outcome scores across all groups and time points for all participants.

	Psilocybin		Placebo	
	Baseline	Four-Week	Baseline	Four-Week
VAS PLP	5.56 (1.34)	3.76 (1.53)	8.07 (0.47)	7.20 (1.40)
VAS residual	6.90 (0.79)	2.6 (1.36)	3.80 (1.91)	5.70 (1.98)
BPI interference	2.54 (1.18)	1.51 (1.28)	3.50 (1.14)	4.43 (1.60)
BPI Severity	3.9 (0.90)	1.80 (0.95)	3.38 (0.96)	3.25 (1.02)

VAS = Visual analog scale; PLP = Phantom limb pain; BPI = Brief pain inventory; mean (SD)

Recent Review Articles. See References 1–6.

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Notes

The author declares no competing financial interest.

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