

Concomitant use of antidepressants and classic psychedelics: A scoping review

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Abstract

Classic psychedelics are increasingly studied as potential treatments for different psychiatric disorders. Current research protocols often require patients to discontinue antidepressants (ADs) for at least 2 weeks before psychedelic administration to decrease the risk of serotonin syndrome and limit their effect on efficacy and the acute subjective effects of psychedelics. Moreover, the discontinuation of ADs represents a significant burden to patients that could also worsen their depression status and increase suicidal ideation. Together, this suggests that the general recommendation for AD discontinuation might be unnecessary and even detrimental to the therapeutic efficacy of psychedelics. In this scoping review, we summarise the existing literature on the concomitant use of conventional ADs with classic psychedelics in humans with the aims to assess safety, tolerability, efficacy, and subjective effects. Following PRISMA-ScR guidelines, we searched MEDLINE, Embase, and Scopus databases to retrieve relevant literature from inception to March 3, 2025. Data were systematically charted from included studies. We included 18 studies and found that the concomitant use of ADs and classic psychedelics is generally safe and tolerable, with no increased risk of serotonin syndrome, particularly for psilocybin. Some studies reported significant improvements in depression and other mental health symptoms. While some evidence indicates a potential attenuation of acute subjective psychedelic effects, this was not observed in all studies. Accordingly, we

conclude that the use of ADs can be maintained to enhance patient access to psychedelic treatments and avoid the risk of AD discontinuation syndrome. Finally, this review highlights limitations and several knowledge gaps in the current literature that need to be addressed in future randomized double-blind, placebo-controlled trials.

Keywords: antidepressants; classic psychedelics; safety; subjective effects; treatment efficacy.

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