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# Regarding "The molecular mechanisms through which psilocybin prevents suicide: evidence from network pharmacology and molecular docking analyses"

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Clinical investigations into the therapeutic actions of psilocybin have been the focus of much attention in recent years as duly cited in the manuscript. The authors of the present manuscript discuss potential targets through which psilocybin may help prevent suicide using computational network pharmacology coupled with molecular docking investigations.

Unfortunately, the manuscript contains the following oversight: Psilocybin is rapidly converted to psilocin in plasma – i.e., psilocybin is a prodrug of psilocin, see Fig. 1 [1].

The acute subjective effects of psilocybin are correlated with the plasma concentration and serotonin 2 A receptor occupancy of psilocin [2] and the authors also reference this study in the manuscript (Reference 66). Therefore, any therapeutic effects elicited by psilocybin can be attributed to the active metabolite psilocin, and potentially the metabolites of psilocin – not psilocybin. Furthermore, CryoEM structures of Psilocin in complex with the serotonin 2 A receptor are also available [3].

Thus, the discussion on the binding of psilocybin to various proteins in the present manuscript is nonsensical in the context of trying to shed light on the therapeutic effects of Psilocybin in humans.

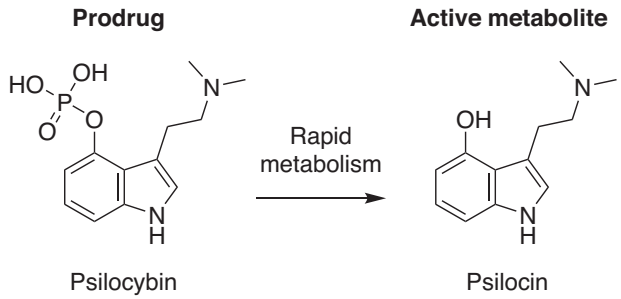


**Fig. 1** Psilocybin is a prodrug that is rapidly dephosphorylated to the active metabolite psilocin.

## REFERENCES

1. Holze F, Becker AM, Kolaczynska KE, Duthaler U, Liechti ME. Pharmacokinetics and Pharmacodynamics of Oral Psilocybin Administration in Healthy Participants. Clin Pharmacol Ther. 2023;113:822–31. https://doi.org/10.1002/cpt.2821.
2. Madsen MK, Fisher PM, Burmester D, Dyssegaard A, Stenbæk DS, Kristiansen S, et al. Psychedelic effects of psilocybin correlate with serotonin 2A receptor occupancy and plasma psilocin levels. Neuropsychopharmacology. 2019;44:1328–34. https://doi.org/10.1038/s41386-019-0324-9.
3. Gumpper RH, Jain MK, Kim K, Sun R, Sun N, Xu Z, et al. The structural diversity of psychedelic drug actions revealed. Nat Commun. 2025;16:2734. https://doi.org/10.1038/s41467-025-57956-7.

## AUTHOR CONTRIBUTIONS

All contributions to the present manuscript were made by the author.

## COMPETING INTERESTS

The authors declare no competing interests.

## ADDITIONAL INFORMATION

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