

**ONTARIO COURT OF JUSTICE  
(South West Region)**

**B E T W E E N:**

**HIS MAJESTY THE KING**

**Respondent**

**- and -**

**SAMER AKILA**

**Applicant**

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**AFFIDAVIT OF PROFESSOR DAVID NUTT**

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I, Professor David Nutt, of the city of Bristol in England, MAKE OATH AND SAY/AFFIRM:

1. I acknowledge that it is my duty to provide evidence in relation to this proceeding as follows:
  - (a) to provide opinion evidence that is fair, objective and non-partisan;
  - (b) to provide opinion evidence that is related only to matters that are within my area of expertise; and
  - (c) to provide such additional assistance as the court may reasonably require, to determine a matter in issue.
2. I acknowledge that the duty referred to above prevails over any obligation which I may owe to any party by whom or on whose behalf I am engaged.
3. I am offering myself as an expert on the effects of psilocybin, the safety of psilocybin and the safety of psilocybin relative to the safety of other recreational drugs.

Personal Qualifications

4. Attached hereto and marked as exhibit A is a true copy of my CV.

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5. I am a psychiatrist and professor of Neuropsychopharmacology at Imperial College London.
6. I have worked for almost all my professional life in psychiatry with a particular interest in psychopharmacology. This topic covers the effects, both beneficial and harmful, of drugs on the brain. I have extensive clinical and research experience in this field and in 2024 Scholar GPs ranked me as leading psychopharmacologist in the world.<sup>1</sup>
7. I am a Fellow of the Royal Colleges of Physicians and of Psychiatrists, the British Pharmacological Society and the Academy of Medical Sciences of the UK.
8. Because of my expertise in drugs of potential abuse I was appointed to chair the UK government Advisory Council on the Misuse of Drugs Technical sub-committee for the assessment of drug harms from 1999-2008. As a result of my long and effective contribution to drug policy in the UK I was appointed to Chair of the full ACMD Council in 2008.
9. In 2004/5 I was the medical lead on the UK government's Foresight committee that provided a 25-year future vision of addiction and brain science. This report was so well received that it was published as a book.<sup>2</sup>
10. I have published over 500 research papers as well as several hundred specialist reviews and over 30 books in this field largely on the effects of drugs on the brain (see cv). My book on drugs for the general public – *Drugs: without the hot air*<sup>3</sup> (UIT press) won the UK Transmission prize for science communication in 2014. Since then, I have written a 2<sup>nd</sup> edition. In 2023 my latest book *Psychedelics*<sup>4</sup> was published in the UK and in 2024 in the USA. Also, in 2023 I published a book on the clinical uses of psychedelics in psychiatry.<sup>5</sup>

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<sup>1</sup> <https://scholargps.com/scholars/73699337611906/david-j-nutt>

<sup>2</sup> Nutt, D.J., Robbins, T.W., Stimson, G.V. et al. (2006). *Drugs and the future: Brain science, addiction and society*. Elsevier.

<sup>3</sup> Nutt, D.J. (2012). *Drugs: Without the hot air*. UIT press.

<sup>4</sup> Nutt, D.J. (2024). *Psychedelics*. Hachette Go press.

<sup>5</sup> Nutt, D.J., & Castle, D. (2023). *Psychedelics as psychiatric medications*. Oxford University Press.

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11. Several of my research papers relating to drug harms and policy responses using the Multi Criteria Decision Analysis (MCDA) approach<sup>6 7 8</sup> have been extensively cited and have been used to produce evidence-based changes to national drug policies in several countries including the USA, Finland, Sweden and New Zealand. As a result of this work, I have been asked to speak on comparative drug harms in a number of important locations including at the UN Office of Drugs and Crime, the Houses of Parliament (UK), the European Commission, and in both the Dutch and New Zealand legislatures.
12. For over 25 years acted as the editor of the Journal of Psychopharmacology one of the top journals in the world on the effects of drugs and the brain. Now I edit the journal Drug Science, Policy and Law.
13. In 2013 I was awarded the Nature/Sense About Science annual John Maddox prize for Standing up for Science for “pursuing research of public interest with perseverance and courage.”
14. My expertise has been recognised with a number of prestigious appointments including Presidencies of the European Brain Council (2013-2017) and of the European College of Neuropsychopharmacology, the British Association of Psychopharmacology and the British Neuroscience Association. I have also served on the MRC Neuroscience board, and for 16 years I held programme grant funding from the MRC for the study of addictions and the effects of drugs on the brain.
15. I have conducted scientific research on the brain actions in humans of a wide range of legal and illegal drugs including psilocybin, alcohol, tobacco, heroin, cocaine, GHB, buprenorphine, antidepressants, benzodiazepines, antipsychotics, methadone, LSD,

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<sup>6</sup> Nutt, D.J., King, L.A., Saulsbury, W., et al. (2007). Development of a rational scale to assess the harm of drugs of potential misuse. *The Lancet*, 369, 1047-1053.

<sup>7</sup> Nutt, D.J., King, L.A., & Phillips, L.D. (2010). Independent scientific committee on drug harms in the UK: A multicriteria decision analysis. *Lancet*, 376(9752), 1558-1565.

<sup>8</sup> van Amsterdam, J., Nutt, D.J., Phillips, L., et al. (2015). European rating of drug harms. *Journal of Psychopharmacology* 29(6), 655-660.



amphetamines, DMT, cannabis, cannabidiol, ketamine, paracetamol, ibuprofen and caffeine.

16. I have also studied the effects on the brain of the impact of repeated use of a range of illegal drugs including psilocybin, LSD cocaine, heroin and cannabis and compared them with the harms of alcohol.
17. Over the past decade I have led a research group studying the impact of psychedelic drugs on human brain using both psychological and neuroimaging measures. We have studied psilocybin, LSD, DMT and currently 5-MEO-DMT.
18. This work led to the development of studies to explore the clinical utility of psilocybin in psychiatric disorders. We have conducted studies in treatment-resistant depression, OCD, anorexia nervosa and fibromyalgia. Currently we are setting up the world's first study of psilocybin in abstinent heroin addicts and in gambling addiction.
19. This body of research work has led to over 100 peer reviewed published papers making us the leading psychedelic research group in the world.
20. I declare that I have no competing interests in that I do not work for any company that is developing psilocybin as a medicine nor do I have any shares or ownership in any psilocybin-related companies. However, our research group has received funds, in kind, from companies making psilocybin for clinical research.
21. I have been asked to prepare an expert report on the effects of psilocybin as per the following questions:
  - a. Can a person who consumed psilocybin reasonably expect to potentially experience any of the following thought-related effects during or after their psilocybin experience: cognitive flexibility, spirituality, life-meaning, connectivity, ego dissolution, empathy, compassion, mindfulness, creativity or other similar effects?



- b. What are the biological and physiological effects of taking psilocybin and how do these effects promote cognitive enhancement and other beneficial effects listed in question #1? Please consider neuroplasticity and the default mode network.
- c. What are the health and safety risks from consuming psilocybin?

## MY OPINION

### Background of psilocybin

- 22. Psilocybin is an alkaloid obtained from a range of fungi – collectively known as magic mushrooms. Psilocybin is not active until broken down in the body to psilocin, the active compound.
- 23. Over 100 species have been identified and they are found all over the world.
- 24. Psilocybin magic mushrooms are known to have been consumed for at least 7 millennia as are represented in some of the earliest human art and sculpture. They were important elements of the annual Ancient Greek Eleusinian ceremonies that ran from 1000 BC to about 400 AD. There is evidence of spiritual use in South and Latin Americas for several millennia.
- 25. Recent research has revealed the pharmacology of psilocybin/psilocin to be through the stimulation of a subtype of serotonin (5-HT) receptor in the brain – the 5-HT<sub>2A</sub> receptor. This effect lasts about 5 hours following oral dosing, though much less if it is given i.v.
- 26. Dosing levels: psilocybin can be taken at a range of doses: high (macro), medium (midi) or low (mini) or very low (micro) doses.

Can a person who consumed psilocybin reasonably expect to potentially experience any of the following thought-related effects during or after their psilocybin experience: cognitive flexibility, spirituality, life-meaning, connectivity, ego dissolution, empathy, compassion, mindfulness, creativity or other similar effects?

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27. There is considerable scientific evidence to support the following effects of psilocybin in both healthy volunteers and some patient groups.

- a. Cognitive flexibility. This is the improved ability to engage with and alter thinking processes, especially to escape from or terminate depressive ruminations.<sup>9</sup> This subjective experience is supported by brain imaging studies that reveal the brain is more flexible (less modular) after a psilocybin treatment.<sup>10</sup> Attached hereto and marked as exhibit B is a copy of Watts, et al. 2017 which I accept and adopt as part of my evidence.
- b. Spirituality.<sup>11</sup> Attached hereto and marked as exhibit C is a copy of Griffiths, et al. 2008 which I accept and adopt as part of my evidence except for the 4<sup>th</sup> paragraph down on page 10. That paragraph relies on outdated science.
- c. Life meaning. Many people state that a psilocybin trip is one of the most personally meaningful experiences of their lives. The state of wonder and altered thinking that can emerge in a psilocybin trip is often seen as being very meaningful and spiritual. This occurs not only in people seeking treatment for mental illness<sup>12</sup> but also in healthy volunteers.<sup>13</sup>
- d. Connectivity with self, others and with nature.<sup>14 15</sup>
- e. Ego-dissolution. This is the experience that one's sense of self or ego is diminished during the psilocybin trip. In the extreme case it can lead people to feel that they

<sup>9</sup> Watts, R., Day, C., Krzanowski, J., et al. (2017). Patients' accounts of increased "connectedness" and "acceptance" after psilocybin for treatment-resistant depression. *Journal of Humanistic Psychology*, 57, 520-564.

<sup>10</sup> Daws, R., Timmerman, C., Giribaldi, B., et al. (2022). Decreased brain modularity after psilocybin therapy for depression. *Nature Medicine*, 28, 844-851.

<sup>11</sup> Griffiths, R., Richards, W., Johnson, M., et al. (2008). Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. *Journal of Psychopharmacology*, 22(6), 621-632.

<sup>12</sup> Watts, R., Day, C., Krzanowski, J., et al. (2017). Patients' accounts of increased "connectedness" and "acceptance" after psilocybin for treatment-resistant depression. *Journal of Humanistic Psychology*, 57, 520-564.

<sup>13</sup> Lyons, T., & Carhart-Harris, R.L. (2018). Increased nature relatedness and decreased authoritarian political views after psilocybin for treatment-resistant depression. *Journal of Psychopharmacology*, 32(7), 811-819.

<sup>14</sup> Watts, R., Day, C., Krzanowski, J., et al. (2017). Patients' accounts of increased "connectedness" and "acceptance" after psilocybin for treatment-resistant depression. *Journal of Humanistic Psychology*, 57, 520-564.

<sup>15</sup> Lyons, T., Carhart-Harris, R.L. (2018). Increased nature relatedness and decreased authoritarian political views after psilocybin for treatment-resistant depression. *Journal of Psychopharmacology*, 32(7), 811-819.

have moved into other spaces, places and even other dimensions of universes, or that their body is being atomized and floating out of its normal existence.<sup>16</sup>

- f. Empathy and compassion.<sup>17</sup>
- g. Mindfulness – the sense that the person is more able to regulate internal thought processes, especially to suppress or eliminate ones that are counterproductive and self-critical. The ability to control or escape from inner dialogues.<sup>17 18</sup>
- h. There is less good evidence for creativity.

What are the biological and physiological effects of taking psilocybin and how do these effects promote cognitive enhancement and other beneficial effects listed in question #1? Please consider neuroplasticity and the default mode network.

28. The 5-HT<sub>2A</sub> receptors that mediate the effects of psilocybin are more highly expressed in the human brain compared with all other animals. They are most highly expressed on the layer 5 neurons in the cortex, which are responsible for integrating cortical function. 5-HT<sub>2A</sub> receptors are most dense in the most recently evolved parts of the human brain – the transmodal cortex. This is the brain network in which human-specific cognitive processes such as abstract and creative thinking, imaging and self-reflection take place.<sup>19</sup>

29. By stimulating these layer 5-HT<sub>2A</sub> receptors psilocybin (and other serotonergic psychedelics) disrupt ongoing rhythmic activity of the brain leading to much less synchronised brain activity, a state we call the entropic brain.<sup>20 21</sup> The entropic state is one

<sup>16</sup> Lebedev, A.V., Lövdén, M., Rosenthal, G., et al. (2015). Finding the self by losing the self: Neural correlates of ego-dissolution under psilocybin. *Human Brain Mapping*, 36(8), 3137-3153.

<sup>17</sup> Watts, R., Day, C., Krzanowski, J., et al. (2017). Patients' accounts of increased "connectedness" and "acceptance" after psilocybin for treatment-resistant depression. *Journal of Humanistic Psychology*, 57, 520-564.

<sup>18</sup> Griffiths, R., Richards, W., Johnson, M., et al. (2008). Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. *Journal of Psychopharmacology*, 22(6), 621-632.

<sup>19</sup> Luppi, A.I., Girn, M., Rosas, F.E., et al. (2024). A role for the serotonin 2A receptor in the expansion and functioning of human transmodal cortex. *Brain*, 147(1), 56-80.

<sup>20</sup> Carhart-Harris, R.L., Erritzoe, D.E., Williams, T.M., et al. (2012). The neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. *Proceedings of the National Academy of Sciences of USA*, 109(6), 2138-2143.

<sup>21</sup> Carhart-Harris, R.L., & Friston, K.J. (2019). REBUS and the anarchic brain: Toward a unified model of the brain action of psychedelics. *Pharmacological Reviews*, 71(3), 316-344.

in which the regular rhythmic activity of the brain is markedly reduced so allowing increases connectivity between brain regions and so a different level(s) of consciousness. The entropic state usually brings more positive and functional changes to the brain. Because the entropic state breaks down established ways of thinking it allows people to think in more creative and diverse ways.

30. These changes can explain many aspects of the psychedelic state (or trip) such as hallucinations, out of body experiences, wonder and personal insights.<sup>22</sup>
31. Psilocybin-induced desynchronized brain activity then allows significantly increased connectedness between brain regions.<sup>23</sup> Neuroimaging studies reveal that this increased connectivity persists for at least 3 weeks after a single psilocybin dose.<sup>24</sup>
32. Consonant with the neuroimaging studies referred to in point 31 that reveal enhanced functional connectivity across the brain for a period after the acute experience (trip) people often report improved mental wellbeing, improved cognitive flexibility and with an enhanced sense of being more connected with others, with nature and with the world.<sup>25</sup>
33. Of particular relevance was the novel neuroimaging discovery that psilocybin administration leads to a breakdown of a brain network called the Default Mode Network (DMN). This network encodes all aspects of a person's sense of self, both in terms of location in time and space as well as in terms of self-value. Some would say it is the location for the ego.
34. There is evidence that the DMN is over-engaged in people with mental illness such as depression in which repetitive thought loops (ruminations) dominate thinking and are

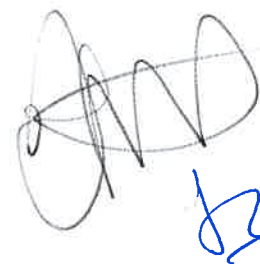
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<sup>22</sup> Carhart-Harris, R.L., Erritzoe, D.E., Williams, T.M., et al. (2012). The neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. *Proceedings of the National Academy of Sciences of USA*, 109(6), 2138-2143.

<sup>23</sup> Petri, G., Expert, P., Turkheimer, F., et al. (2014). Homological scaffolds of brain functional networks. *Journal of the Royal Society Interface*, 11(101), 20140873.

<sup>24</sup> Daws, R., Timmerman, C., Giribaldi, B., et al. (2022). Decreased brain modularity after psilocybin therapy for depression. *Nature Medicine*, 28, 844-851.

<sup>25</sup> Watts, R., Day, C., Krzanowski, J., et al. (2017). Patients' accounts of increased "connectedness" and "acceptance" after psilocybin for treatment-resistant depression. *Journal of Humanistic Psychology*, 57(5), 520-564.



beyond voluntary control.<sup>26</sup> This can happen to a lesser extent to healthy normal people who sometimes feel depression or anxiety.

35. In such people the entropic state that arises from psilocybin treatment disrupts the DMN and in the post-treatment period it is less self-engaged and is more connected with other brain networks especially the executive and salience ones.<sup>27</sup> This allows more normal functional, i.e., less depressed, brain activity. Though less studied at present I believe that similar functional changes underpin the value of psilocybin in other mental illnesses such as OCD and anorexia in which over-entrenched thought loops drive behavior. A very recent as yet unpublished study of ours has found that such improvements in network connectivity occur after a single psilocybin trip in people without a mental illness diagnosis, last for at least a month, and their magnitude correlates with improvement in wellbeing.

36. A further neuroscience discovery with psilocybin (and other serotonergic psychedelics) is that for some time after their administration a state of facilitated neuroplasticity is found. This is revealed by the growth of new neural processes (dendrites) and synapses, seen in rodent models.<sup>28</sup> It is believed that these neuroplastic processes allow improved learning of new mental states that emerge during the treatment.

#### What are the health and safety risks from consuming psilocybin

37. Historically magic mushrooms have been used by many millions of people over thousands of years with very few reports of significant harms. In recently times use in Western countries has become popular with little evidence of significant harms.<sup>29</sup>

38. Typically, the doses used in these exposures are designed to produce a psychedelic experience i.e. a trip – so these are known as macrodoses.

<sup>26</sup> Berman, M., Peltier, S., Nee, D., et al. (2011). Depression, rumination and the default network. *Social Cognitive and Affective Neuroscience*, 6(5), 548–555.

<sup>27</sup> Daws, R., Timmerman, C., Giribaldi, B., et al. (2022). Increased global integration in the brain after psilocybin therapy for depression. *Nature Medicine*, 28, 844–851.

<sup>28</sup> de la Fuente Revenga, M., Zhu, B., Guevara, J., et al. (2021). Prolonged epigenomic and synaptic plasticity alterations following single exposure to a psychedelic in mice. *Cell Reports*, 37(3), 109836.

<sup>29</sup> van Amsterdam, J., Opperhuizen, A., & van den Brink, W. (2011). Harm potential of magic mushroom use: A review. *Regulatory Toxicology and Pharmacology*, 59(3), 423–429.

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39. There are several different ways in which psilocybin and psilocybin-containing magic mushrooms are used. These are most commonly as a large trip-inducing dose called a macrodose (about 25 mg psilocybin) and as a very small non-psychedelic dose called a microdose (1mg or less). In some clinical setting an intermediate dose called a mididose (5-10mg) of psilocybin is used to facilitate psychotherapy.
40. Microdosing psilocybin has become popular in recent years. This usually takes the form of using dried magic mushrooms on a daily or two-three times a week basis.<sup>30</sup> Strictly microdosing means the dose is below a subjectively detectable level though in many cases users take enough to have a just-detectable effect so they can be sure they are getting a pharmacological action in their brain (sometimes called a minidose).
41. Microdosing is used to promote wellbeing and improve cognitive and creative performance. There is a great deal of anecdotal evidence of the value of microdosing. However, due largely to the barriers to research that the legal status of psilocybin and magic mushrooms brings, few rigorous academic studies of microdosing have been conducted. At present we cannot say there is proof that psilocybin microdosing has more efficacy than placebo.<sup>30</sup>
42. Synthetic psilocybin was released as a research medicine (called Indocybin) from 1958-1966 by Sandoz again with no evidence of significantly adverse effects resulting.
43. In modern trials over 1000 patients have been treated with psilocybin without significant harms emerging<sup>31</sup> consistent with the earlier clinical data. To my knowledge there have been few if any cases of the treatment actually worsening the condition. Similarly, there are no reported cases of healthy volunteers experiencing an emergence of a psychiatric state following a research treatment with psilocybin. Systematic assessments of psilocybin harms compared with other psychoactive drugs have recently been conducted by four independent groups using state of the art methodology – multi criteria decision making.<sup>32</sup> Attached

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<sup>30</sup> Rootman, J.M., Kryskow, P., Harvey, K., et al. (2021). Adults who microdose psychedelics report health related motivations and lower levels of anxiety and depression compared to non-microdosers. *Scientific Reports*, 11, 22479.

<sup>31</sup> Schlag, A., Aday, J., Salam, I., et al. (2022). Adverse effects of psychedelics: From anecdotes and misinformation to systematic science. *Journal of Psychopharmacology*, 36(3), 258-272.

<sup>32</sup> Nutt, D.J., King, L.A., & Phillips, L.D. (2010). Drug harms in the UK: A multicriteria decision analysis. *The Lancet*, 376(9752), 1558–1565; van Amsterdam, J., Nutt, D.J., Phillips, L., et al. (2015). European rating of drug harms. *Journal of Psychopharmacology*, 29, 655–660; Bonomo, Y., Norman, A., Biondo, S., et al. (2019). The

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hereto and marked as exhibit D is a copy of Nutt, et al. 2010 which I accept and adopt as part of my evidence. Attached hereto and marked as exhibit E is a copy of Bonomo, et al. 2019 which I accept and adopt as part of my evidence. Attached hereto and marked as exhibit F is a copy of Schlag, et. al. 2022 which I accept and adopt as part of my evidence.

44. The MCDA approach defines the harms of drugs and then compares them for many different ones – see Table – The 16 different harms of drugs.

**Harms to assess**

1. Drug-specific mortality
2. Drug-related mortality
3. Drug-specific harms
4. Drug-related harms
5. Dependence
6. Drug-specific impairment of mental functioning
7. Drug-related impairment of mental functioning
8. Loss of tangibles
9. Loss of relationships

**Harms to address**

1. Injury
2. Crime
3. Economic cost
4. Impact on family life
5. International damage
6. Environmental damage
7. Decline in reputation of the community

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Australian drug harms ranking study. *Journal of Psychopharmacology*, 33, 759–768; Crossin, R., Cleland, L., Wilkins, C., et al. (2023). The New Zealand drug harms ranking study: A multi-criteria decision analysis. *Journal of Psychopharmacology*, 37(9), 891-903.



## Drugs ranked according to total harm

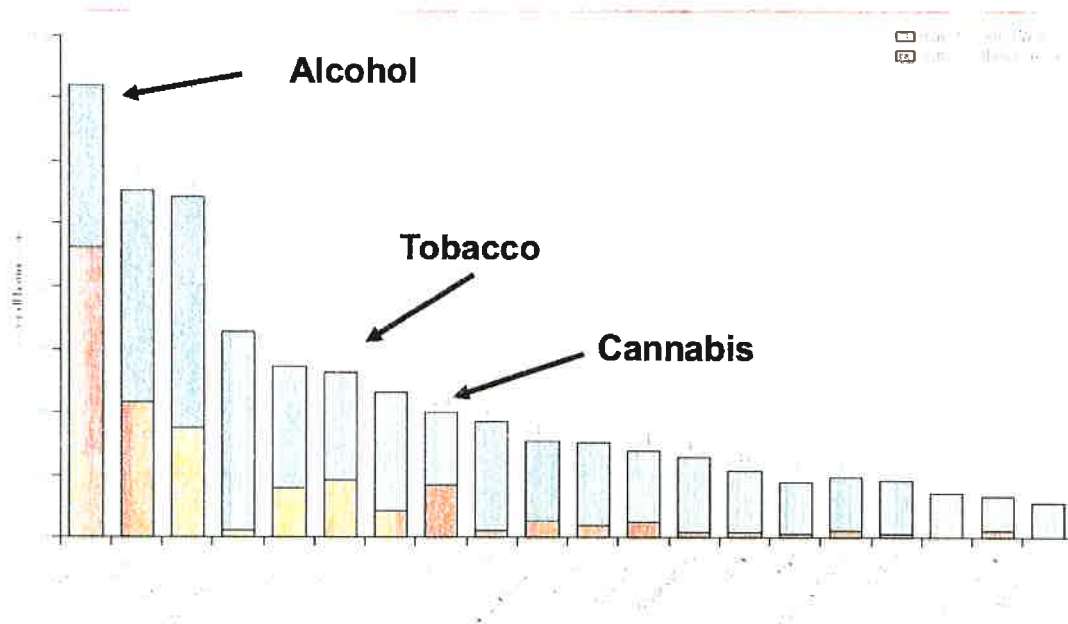


Figure 2. Drugs ordered by their overall harm scores, showing the separate contributions to the overall scores of harms to users and neighbours. (Nutt, King & Phillips, 2010)

Nutt, King & Phillips Lancet Nov 2010

45. All four studies concluded that psilocybin was one of the least harmful drugs when used recreationally. These harms are predicted to be even lower in medical settings.
46. Of particular note is that alcohol scores much more highly in comparison with psilocybin in all these assessments.
47. A major reason for the low harms of psilocybin is the fact that it is used only intermittently – often just once.
48. The long-term use of microdosing contrasts with that of macrodosing though there are no formal long-term studies of the safety of microdosing the doses are so low as to be very unlikely to have significant negative health effects.
49. Risks of macrodosing, i.e. using psilocybin to produce a psychedelic state.

- a. The mental contents of the psychedelic state are unpredictable and can lead people to think and behave very differently to how they usually do. In theory this can lead to them coming to accidental harm through disregarding or misinterpreting risks associated with an action or behaviour. It is also possible they might induce beliefs that lead to self-harmful acts.
- b. Such examples with psilocybin are very rare and have not been reported in the current series of modern trials in over 1000 patients and a similar number of healthy volunteers. In all of these exposures the subjects take the psilocybin in a safe locality and in the presence of a non-treated responsible adult.
- c. Data on magic mushrooms is available from the UK government's annual survey on deaths from a range of recreational drugs.<sup>33</sup> It is estimated that about a quarter of a million people a year in the UK use magic mushrooms.<sup>34</sup> Only one fatality possibly linked to their use has been reported in the past 20 years in comparison with over 100,000 from alcohol and more than 20,000 from opioids.
- d. Are people with mental health problems more vulnerable to harms? Clearly risks from the use of any psychoactive substance are greater in people with current and past mental health problems especially psychosis. It is also possible that people with a close (first-degree) family relative with psychosis would also be at greater risk. For these reasons such individuals are currently excluded from research trials with psychedelics including psilocybin.
- e. Beyond psychosis the major predictor of poor or negative outcomes from psilocybin is the presence of anxiety before and during the treatment. This

<sup>33</sup><https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/adhocs/13746drugrelateddeathregistrationsmentioningpsilocybinenglandandwales1993to2020>.

<sup>34</sup><https://www.ons.gov.uk/peoplepopulationandcommunity/crimeandjustice/articles/drugmisuseinenglandandwales/yearendingmarch2023>.



- can be overcome by good education and preparation and the presence of a non-tripping therapist or friend during the experience.
- f. Screening prior to the use of psilocybin, for example by the person's doctor or a dispensing pharmacist would be one way to mitigate this. Prior safe exposures would also be a relevant consideration.
  - g. An alternative/ complementary approach is to use app-based self-help educational material prior to purchase e.g. as the Dutch psilocybin truffle company Mushrooms and More provide.
  - h. Anxiety is also reduced by knowledge that the supplier is providing the exact and correct dose. It can further be reduced by giving lower doses to those at higher risk of panic attacks, e.g. those with prior history of these or other anxiety disorders.
  - i. Adverse effects of psilocybin are more likely to occur in people who are intoxicated with alcohol and some other drugs e.g. stimulants. Also adverse effects have been reported in people taking some medications such lithium or monoamine oxidase inhibitors. The use of these substances should be avoided in people who use psilocybin.
  - j. Although there are no systematic studies it seems likely that people with brain injury or other neurological conditions might be more vulnerable to adverse effects from psilocybin. For these reasons they are excluded from research with psilocybin.
  - k. One major safety factor for macrodosing psilocybin is that for most people (whether patients or other users) very few doses are used. Adverse effects from chronic use are therefore not seen.

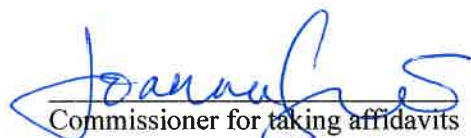
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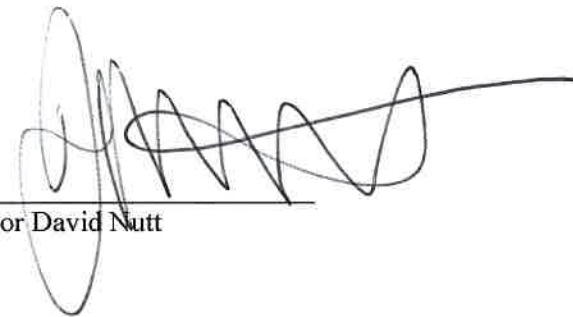
50. Risks of psilocybin when used at microdosing levels. These are very much lower than those for macrodosing as there is little if any impact on mental processes or cognitions other than those wanted/expected by the user.<sup>35</sup>

- a. However, as microdosing tends to be done on a regular daily or 2-3 times weekly basis for months or years there is the question of whether chronic exposure even at such a low/ inactive dose for the brain might have negative effects on other organs. This is especially relevant to the heart and pulmonary circulation where the 5-HT2B receptor is found and stimulation of which can lead to endothelial thickening. Psilocybin has high affinity for this receptor subtype so in theory its use could promote such growths. However, such changes have not been reported so far.

51. Risks of psilocybin when used at midi-dosing levels. These are lower than those for macrodosing as the mental state is not accompanied by hallucinations or other profound perceptual changes. However, in our trials the emotional experience can be profound.

Sworn remotely via video conference )  
 by David Nutt in the city of Bristol, )  
 England, and the commissioner Joanna )  
 Shaw in the city of Toronto, Ontario )  
 this 29<sup>th</sup> day of April 2024. )

  
 Commissioner for taking affidavits  
 Joanna Shaw

  
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 Professor David Nutt

<sup>35</sup> Kuypers, K.P., Ng, L., Erritzoe, D., et al. (2019). Microdosing psychedelics: More questions than answers? An overview and suggestions for future research. *Journal of Psychopharmacology*, 33(9), 1039-1057.