A close-up of a text

AI-generated content may be incorrect.

Nordqvist, C. (2010, November 1). *Alcohol is most harmful drug, followed by heroin and crack*. Medical News Today. https://www.medicalnewstoday.com/articles/206300#1

A graph of drugs

AI-generated content may be incorrect.

The Economist Newspaper. (2019, June 25). *What is the most dangerous drug?*. The Economist. https://www.economist.com/graphic-detail/2019/06/25/what-is-the-most-dangerous-drug

A graph of a number of people

AI-generated content may be incorrect.

Johnson, M. W., Griffiths, R. R., Hendricks, P. S., & Henningfield, J. E. (2018). The abuse potential of medical psilocybin according to the 8 factors of the Controlled Substances Act. *Neuropharmacology*, *142*, 143–166. https://doi.org/10.1016/j.neuropharm.2018.05.012

A screenshot of a document

AI-generated content may be incorrect.

*Alcohol most harmful drug based on multicriteria analysis: Imperial News: Imperial College London*. Imperial News. (2010, November 1). https://www.imperial.ac.uk/news/94042/alcohol-most-harmful-drug-based-multicriteria/

A chart with different colored circles

AI-generated content may be incorrect.

Data source is the March 24, 2007. Nutt, D., King, L. A., Saulsbury, W., & Blakemore, C. (2007). Development of a rational scale to assess the harm of drugs of potential misuse. *The Lancet*, *369*(9566). https://doi.org/10.1016/s0140-6736(07)60464-4

***Neurochemical and Psychophysiological Mechanisms Proposed as a Basis for Ayahuasca’s Effects on Addiction***

***There are a variety of biochemical and physiological mechanisms through which ayahuasca can effectively address addictions (***[***Prickett and Liester, 2014***](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4773875/#B103)***). The inclusion of two plant species in ayahuasca provides a variety of mechanisms for direct and indirect actions on both dopaminergic and serotonergic systems. Since the effects of DMT appear to reflect the general effects of tryptamines (e.g., DMT, LSD, bufotenin, psilocin, and psilocybin) some of therapeutic mechanisms would also be shared with these related substances. The effects of the harmine alkaloids, however, would be unique to ayahuasca. Separate studies with each of these chemical classes will be necessary to distinguish their different contributions.***

[***Liester and Prickett (2012)***](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4773875/#B71) ***proposed that “ayahuasca exerts anti-addictive properties via its direct and indirect actions on dopaminergic and serotonergic neurons in the mesolimbic pathway. Ayahuasca raises global 5-HT levels attenuating withdrawal effects and mitigating against potential dopaminergic excess when utilizing dopamine (DA) agonists. Ayahuasca balances DA in the MDP between the low levels associated with withdrawal and the elevated levels associated with initiation and reinforcement of addictive behavior” (***[***Prickett and Liester, 2014***](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4773875/#B103)***). Therefore, the resolution of addiction through ayahuasca’s therapeutic potentials may act on four levels: (1) reducing brain DA level in the MDP through effects on the 5-HT receptors, which in turn (2) interferes with the synaptic plasticity. This neurochemical mechanism is supported by (3) psychological insights and processing of repressed traumas, enhancing decision making capabilities, which allowing the person to (4) examine first person transcendental experiences.***

***Additional neurophysiologic mechanisms for ayahuasca’s therapeutic effects involve neuroplasticity, the ability of neurons to alter their synaptic connections. Constituents of ayahuasca may affect brain derived neurotropic factor release through effects on the GABAergic and glutamatergic systems. These are involved in producing neuroplastic changes through triggering changes in gene expression which affect the architecture and communication between neurons. These exert effects on the existing neural circuits which mediate maladaptive addictive habits in stimulating the production of new circuits supporting new behaviors, with ayahuasca facilitating a neurological rewiring of the brain’s reward pathways. This model is supported by animal experiments (***[***Oliveira-Lima et al., 2015***](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4773875/#B96)***) which demonstrated that ayahuasca not only inhibits early behaviors associated with the initiation and development of alcohol addiction, but also has long-term effects in preventing the reinstatement of ethanol-induced behavioral sensitization.”***

Frecska, E., Bokor, P., & Winkelman, M. (2016). The therapeutic potentials of ayahuasca: Possible effects against various diseases of civilization. *Frontiers in Pharmacology*, *7*. https://doi.org/10.3389/fphar.2016.00035