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CURRENT ISSUES

Need for a Public Health Response to the Unregulated Sales of *Amanita muscaria* Mushrooms

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INTRODUCTION

Interest in psilocybin-containing mushrooms is increasing in the U.S., with 12.3% of U.S. adults reporting use of psilocybin-containing mushrooms in 2022, up significantly from 11.4% in 2021.[1] This makes psilocybin-containing mushrooms the most commonly used hallucinogenic substance. This growing interest in psilocybin-containing mushrooms has also sparked a new commercial market for other types of mushrooms. Some of these mushrooms have potent pharmacological properties including *Amanita muscaria* mushrooms (Figure 1), which contain the compounds muscimol and its biosynthetic precursor, ibotenic acid. Muscimol is psychotropic (i.e., can produce acute changes in perception, mood, cognition, and behavior), while ibotenic acid is not. Both compounds are also highly toxic and can be fatal at high enough doses. However, unlike psilocybin-containing mushrooms, neither *Amanita muscaria,* muscimol, nor ibotenic acid are scheduled under the 1970 U.S. Controlled Substance Act or comparable international laws in most countries. Herein the history, present availability, safety, and legal status of *Amanita muscaria* are discussed and a case for improved regulation is made in light of serious safety concerns.

A BRIEF HISTORY

Amanita muscaria are widely distributed across temperate and boreal zones of several continents within the Northern Hemisphere, encompassing areas such as the Hindu Kush, Mediterranean basin, and Pacific coasts of the U.S. and Canada.[2] In Siberia, use by old world shamans dates back millennia and predates the crossing of the Bering Straits into North America.[3] Once humans entered North America, *Amanita muscaria* use fell away as new world shamans preferred the use of *Psilocybe spp.* mushrooms found throughout the Americas.

Numerous myths are associated with *Amanita muscaria* mushrooms. Perhaps the most fascinating one is their potential connections to the origin of Santa Claus, which is thought to have originated from rituals performed by shamans in Central Asia in which they are thought to have worn red garments with white trim to collect mushrooms that appeared under spruce trees during the days leading up to the winter solstice.[4] A related belief is that these shamans would feed *Amanita muscaria* mushrooms to reindeer and collect their urine for ceremonial use. This extraction process—if one is generous enough to call it that—was believed to potentiate the effects of *Amanita muscaria* through the hepatic conversion of ibotenic acid to the more potent muscimol in reindeer.[5]

PRESENT AVAILABILITY

Although there is a long history of human use of *Amanita muscaria*, online access to *Amanita muscaria* and muscimol products appears to be a relatively new phenomenon. In the past few years, commercially manufactured products, including harvested *Amanita muscaria* mushrooms and products containing isolated muscimol, have entered the market. Product offerings include candy-flavored muscimol gummies, dessert-flavored muscimol vapes, and pre-rolls blended with hemp flower and muscimol. As one example of the recency and popularity of these products, a single ad for *Amanita muscaria* gummies that was posted on X (formerly Twitter) on

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Figure 1. The *Amanita muscaria* mushroom.
Source: Singleton E. *The Story of the Universe: Told by Great Scientists and Popular Authors*. P.F. Collier and Son; 1905.

July 9, 2023 has already been viewed over 5.5 million times at the time of writing (March 28, 2024).[6] The proliferation of such ads, online retailers, and wholesalers suggests consumer demand may be growing. One method of measuring this demand is through the analysis of Google searches.[7] Google searches related to *Amanita muscaria* rose by 114% from 2022 to 2023 and were 97.4% (95% CI: 78.1–118.3) higher than the expected seasonal trend for 2023 (Figure 2). Please see Appendix (available online) for further description of the analytical methods and data sources used for this Google trends analysis.

INTERSECTION OF *AMANITA MUSCARIA* AND PSILOCYBIN IN CLINICAL RESEARCH

One explanation for the growing interest in *Amanita muscaria* is its potential conflation with emerging clinical research supporting the safety and efficacy of psilocybin as an adjunct to psychotherapy in the treatment of depression. Beginning around 2010, a new era of clinical interest in psilocybin and other "classical psychedelics" emerged, which has been referred to as the "psychedelic renaissance." During this time, the U.S. Food and Drug Administration (FDA) has granted psilocybin breakthrough therapy designations for treatment-resistant depression in 2018 and for major depressive disorder in 2019,[8] and 2 U.S. states (Colorado and Oregon) have legalized psilocybin-assisted psychotherapy programs despite its Schedule I classification under the U.S. Controlled Substance Act.

Some evidence suggests that muscimol may hold therapeutic potential, but this evidence is limited to pre-clinical studies that pursued different treatment applications than those pursued for psilocybin.[9] Nonetheless, *Amanita muscaria* products have been marketed with health-related claims—often by vague references to clinical studies reporting mitigation of anxiety, depression, and other conditions. This marketing violates FDA regulations for labeling claims on food products and dietary supplements; however, the FDA has limited resources, and this may be why they have not initiated enforcement action or communications related to products that contain *Amanita muscaria.*[10]

In this marketplace, there is an important gap between science and growing trends in commerce and culture. This poses risks to consumers given the lack of data supporting the safety of *Amanita muscaria.* It is also heightened because consumers are already turning to *Amanita muscaria* as potential anxiolytics and antidepressants without clinical evidence for these applications.[11] This could prolong symptoms that might otherwise be alleviated by proven therapies.

SAFETY PROFILE OF *AMANITA MUSCARIA*

Increased consumer interest and widespread availability are concerns for public health because *Amanita*

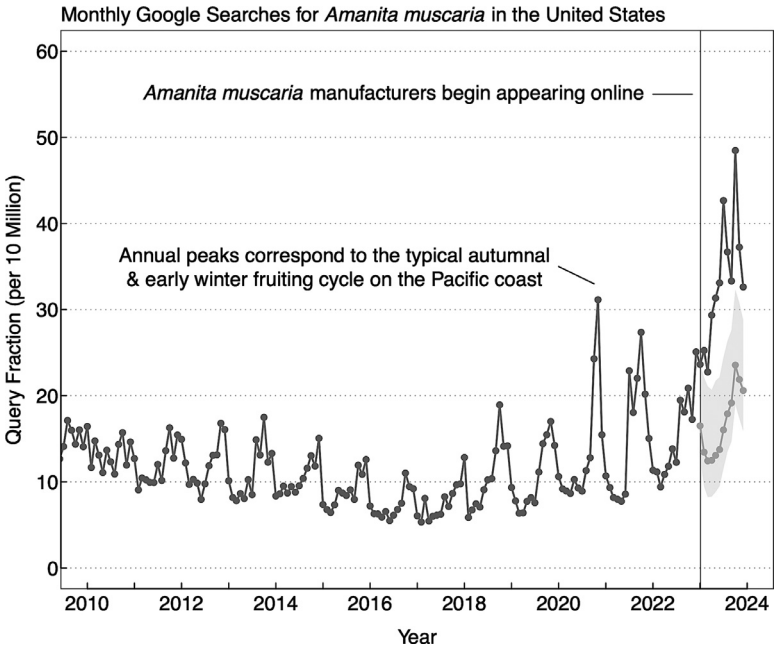

Figure 2. Monthly Google searches for *Amanita muscaria* rise in the U.S.
The figure highlights monthly Google search rates from January 2010 to December 2023 (dark grey line and dots) and expected search rates from January 2023 through December 2023 for the U.S. (light gray line, dots, and polygon). Forecasts were projected through 2023 using an autoregressive integrated moving average model selected by the Hyndman and Khandakar algorithm and monthly trends from January 2010 to December 2022 (see Appendix, available online, for further methodological details).

muscaria products contain compounds that are toxic including muscimol, ibotenic acid, and muscarine.[9] Most scientific literature on the health effects of *Amanita muscaria* in humans pertains to studies of the ingestion of raw *Amanita muscaria* mushrooms. These effects include dizziness, dysphoria, visual hallucinations, agitation, ataxia, muscle fasciculation, seizures, and coma.[12] While death is rare, it has been reported as an outcome, including a case reported in the last year of a 44-year-old man who died after ingesting 4 dried *Amanita muscaria* mushroom caps.[13] The first documented case of hospitalization due to *Amanita muscaria* consumption in the United Kingdom was reported in July 2023.[14] This case involved a 46-year-old woman who had ingested dried mushrooms (0.5 grams) daily for 2 weeks as part of what is referred to as a "microdosing" regimen that was being followed in an attempt to reduce anxiety without inciting psychotropic properties. She reportedly purchased 20 grams of *Amanita muscaria* mushrooms from a website advertised on social media.

ACUTE TOXICITY OF MUSCIMOL AND IBOTENIC ACID

Estimates of the acute toxicities of muscimol and ibotenic acid are available. We compared muscimol and ibotenic acid in relation to available published oral mouse models using LD50 (lethal dose required to kill 50% of the participants in a test population) estimates for other compounds on a list of commonly used psychotropic drugs provided by the U.S. National Institute on Drug Abuse.[15] These estimates, available in Table 1, suggest that the acute toxicities of muscimol and ibotenic acid in oral mouse models are higher (lower LD50) than those of most commonly used psychotropic drugs, including fentanyl, cocaine, and phencyclidine (commonly referred to as PCP). All values and their PubChem IDs and references are available in the Appendix Tables 1 and 2 (available online) as are values for available oral rat models in Appendix Table 3 (available online).

PSYCHOTROPIC PROPERTIES OF MUSCIMOL

The psychotropic effects of *Amanita muscaria* are related to muscimol and not ibotenic acid, which is partially metabolized to muscimol in vivo when consumed.[16] Similar to alcohol and benzodiazepines, muscimol is a $GABA_A$ receptor agonist that exerts inhibitory effects on the central nervous system, primarily in forebrain regions, such as the *caudate, putamen,*

Table 1. Compounds in *Amanita muscaria* Are More Toxic Than Most Commonly Used Drugs

Compound (Brand or common name)	LD50 (mg/kg)
Nicotine (tobacco)	3.34
Amphetamine (Adderall®)	21
Muscimol (*Amanita muscaria*)	22[a]
Ibotenic acid (*Amanita muscaria*)	38[a]
Diazepam (Valium®)	48
Methadone (Dolophine®, Methadose®)	70
Phencyclidine (PCP)	75
Cocaine (Coke/Crack)	99
Loperamide (Imodium®)	105
Methylphenidate (Concerta®, Ritalin®)	150
Pentobarbital (Nembutal®)	170
Chlorodiazepoxide (Librium®)	200
Meperidine (Demerol®)	200
Dextromethorphan (DXM)	210
Codeine (various brand names)	250
Fentanyl (Actiq®, Duragesic®, Sublimaze®)	368
cathinone (Khat)	400
Delta-9-tetrahydrocannabinol (Cannabis)	482
Morphine (Duramorph®, MS Contin®)	524
Mescaline (Peyote)	880
Triazolam (Halicon®)	1080
Flunitrazepam (Rohypnol®)	1200
Oxandrolone (Anadrol®)	1832
Lorazepam (Ativan®)	1850
Delta-8-tetrahydrocannabinol (cannabis)	>2000
Ethanol (alcohol)	3450
Gamma-hydroxybutyrate (GHB)	4800

Note1: Values are LD50 in oral mouse models for the main psychotropic compounds found in *Amanita muscaria* compared with available estimates for active compounds found in other common drugs administered in the same route and species listed on a list of common drugs by the U.S. National Institute of Drug Abuse.
Note2: Some LD50 values were converted to mg/kg to be expressed on the same scale.
Note3: See Appendix Table 2 (available online) for references and Appendix Table 3 (available online) for oral rat model results and references.
LD50 = the lethal dose required to kill half the participants in a test population.
[a]Psychotropic compounds found in *Amanita muscaria*.

thalamus, and *hippocampus*.[17] Muscimol can cause dizziness, nausea, tiredness, a feeling of weightlessness, visual and auditory hypersensitivity, space distortion, unawareness of time, and colored hallucinations.[18] While some of these effects are similar to those associated with "classical psychedelics" like psilocybin, muscimol does not interact with serotonin 5-HT_{2A} receptors, like psilocybin and other "classical psychedelics."

REGULATORY STATUS

As previously mentioned, *Amanita muscaria* and their constituents are not considered controlled substances in most countries. However, some countries, such as the Netherlands, do consider *Amanita muscaria* and *Amanita pantherina* (another species in the *Amanita* genus that contains muscimol) controlled substances.[19] In an effort to provide legal guidance to consumers, some websites offer interpretations of controlled substance laws (Table 2).

Table 2. Sales Restrictions on *Amanita muscaria* and Muscimol Claimed by One Manufacturer as of January 4, 2023

WHO regions	Countries or states that restrict *Amanita muscaria* sales
African Region (AFR)	None reported
Region of the Americas (AMR)	Brazil, U.S. state of Louisiana
South-East Asian Region (SEAR)	Thailand
European Region (EUR)	Romania, Russia, Sweden, The Netherlands, and Ukraine
Eastern Mediterranean (EMR)	None reported
Western Pacific Region (WPR)	Australia

Note: All listed jurisdictions are those where one U.S.-based manufacturer claims *Amanita muscaria* sales are restricted; all other jurisdictions are thus presumed to permit *Amanita muscaria* sales.
WHO Regions, World Health Organization Regions.

Most manufacturers also explicitly claim that *Amanita muscaria* and muscimol can be sold without restriction throughout the U.S. apart from Louisiana, where it is included on a list of prohibited hallucinogenic substances. This interpretation is likely correct in that it is unambiguously legal to possess, pick, and grow *Amanita muscaria* mushrooms given their unscheduled status, but it is unlikely that products derived from *Amanita muscaria* are legally manufactured for commercial use.

Many *Amanita muscaria* and muscimol products are sold and marketed masquerading as food products or dietary supplements. However, there are no FDA-notarized GRAS (Generally Recognized as Safe) or NDI (New Dietary Ingredient) notifications publicly available for these ingredients. There is a possibility that a manufacturer has self-affirmed GRAS, but this designation seems suspect given the safety data reported in the previous section, which identified severe adverse health events that included hospitalizations and deaths. Thus, the *Amanita muscaria* and muscimol products on the market today are in violation of FDA regulations designed to protect public health.

DOES THE CURRENT REGULATORY APPROACH PROTECT CONSUMERS?

Additional public health concerns directly result from the way that *Amanita muscaria* products are sold. First,

there are no mandated protections for children, such as age restrictions, child-resistant closures, maximum dose requirements, and restrictions on product and marketing features that appeal to children (e.g., cartoons), all of which are now required for state-run recreational cannabis programs in the U.S. Second, although many manufacturers claim to test their products for the amount of active constituents and contaminants, currently there are no accepted testing standards for muscimol or benchmarks for potency. This could lead to inaccurately labeled products. This issue has been found in other consumer products occupying a gray legal market, such as hemp-derived cannabidiol products.[20]

CONCLUSIONS AND RECOMMENDATIONS

A new regulatory approach is needed for *Amanita muscaria* and muscimol-containing products. First, federal and state regulators need to take a clear stance on whether it is legal to commercially manufacture and distribute such products. If this practice is deemed legal, regulatory standards including age restrictions, childproofing, maximum doses, and restrictions on marketing that appeals to children (e.g., cartoons) are needed. Additionally, reference standards and analytical chemistry methods are needed to guide appropriate testing of products to ensure accurate labeling for content to ensure consistent potency and absence of other toxins. Second, it is also crucial that mental health professionals help their patients distinguish between substances like psilocybin, which is being studied for its potential to treat depression, and *Amanita muscaria*, which carries higher toxicity and does not have clinical evidence supporting its use for any health conditions. Given the substantial risks associated with the consumption of *Amanita muscaria* products, it is a "buyer beware" marketplace where consumers are at risk and manufacturers are profiting from delayed regulatory enforcement. The time for a public health first response is now.

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SUPPLEMENTAL MATERIAL

Supplemental materials associated with this article can be found in the online version at https://doi.org/10.1016/j.amepre.2024.05.006.

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Supplemental Online Content

Leas EC, Satybaldiyeva N, Kepner W, Yang KH, Harati RM, Corroon J, Rouffet M. Need for a Public Health Response to the Unregulated Sales of Amanita muscaria Mushrooms, American Journal of Preventive Medicine

Appendix 1. Further description of analytical methods used for Google trends analysis.

Appendix Table 1. The psychoactive compound of the drugs listed in a list of common drugs from the US National Institute on Drug Abuse and an indication of whether these have PubChem records or acute effect estimates.

Appendix Table 2. PubChem records for those with LD50 values in oral mouse models for the main psychedelic compounds found in Amanita muscaria and available estimates in active compounds found in other common drugs administered in the same route and species listed in a list of common drugs by the US National Institute of Drug Abuse

Appendix Table 3. PubChem records for those with LD50 values in oral rat models for the main psychedelic compounds found in Amanita muscaria and available estimates in active compounds found in other common drugs administered in the same route and species listed in a list of common drugs by the US National Institute of Drug Abuse

This supplemental material has been provided by the authors to give readers additional information about their work.

Appendix 1. Further description of analytical methods used for Google trends analysis.

Google Trends data

Google Trends is a publicly available tool that provides access to estimates of actual search requests made to Google either through a dashboard (trends.google.com) or application programming interface (API) called Google Health Trends. These are anonymized (no one is personally identified) and aggregated (grouped together) and have been widely used to measure public interest in consumer goods.[1] These trends allowed us to measure public interest in *Amanita muscaria* using the keyword: amanita muscaria. We obtained the monthly trend in queries from Google Health Trends, accessed through using the Google API Client library in Python [2] from January 2010 through December 2023. The Google Health Trends API reports these measurements as query fractions (QFs), which in our case is the number of searches containing *Amanita muscaria* originating in the time frame divided by the total number searches in the same time frame and geography and expressed in per 10 million searches.

ARIMA model selection and evaluation

We forecasted monthly *Amanita muscaria* searches from January 2023 through December 2023 using an autoregressive integrated moving average (ARIMA) model and data from all months since January 2010, the beginning of the so-called "psychedelic renaissance" to December 2022, the last month before an *Amanita muscaria* extract manufacturer came online. ARIMA models aim to improve over simpler time-series regression models by describing the auto-correlation in the data as well as trends, and then incorporating this information into the projection.[3] An ARIMA model has three components: an autoregressive component of order p, a pre-processing component which differences the data of order d, and an error term given by a moving average of

order *q*, expressed with the syntax ARIMA(p, d, q). A seasonal ARIMA model is formed by including additional seasonal terms in the ARIMA models for the components we have just introduced. The seasonal part of the model consists of the same terms as the ARIMA model, but involves backshifts in the seasonal trend rather than, in our case, the monthly trend. It is expressed with ARIMA(p, d, q)(P, D,Q)[m] where m defines the time period where the pattern repeats–e.g., 12 in our case because we identified a pattern that repeats yearly and we obtained monthly data. We selected our ARIMA by using the historical search trends and the Hyndman-Khandakar algorithm, implemented using the auto.arima() function in the "forecast" package in R. [4] This algorithm combines unit root tests to determine the value of *d*, followed by minimization of the sample-size-adjusted Akaike Information Criterion to select values of *p*, *q* for both the monthly and seasonal components. The final ARIMA model specifications selected by the Hyndman-Khandakar algorithm in our case was ARIMA(1,1,1)(0,1,1)[12].

Forecasting expected volumes through 2023

We then used this ARIMA model to make forecasts of monthly *Amanita muscaria* searches from January 2023 through December 2023, using the forecast function from the "forecast" package [4]. Specifically, the residual values from the model were resampled to simulate n = 10,000 possible "future paths" that included the addition of error for new simulated observations as the time horizon increased, allowing for increasing uncertainty at future time points. [5] We plot the predictions using the median and the 2.5th and 97.5th percentiles of the forecast paths, representing 95% prediction intervals.

Testing the difference between observed and expected search volumes in 2023

We compared the difference in observed and expected search rates after the first *Amanita muscaria* manufacturer appeared to come online with expected volumes calculated as described in the previous section. We calculated the cumulative excess or dearth in search volume for the period with bootstrap 95% Confidence Intervals.

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Appendix Table 1. The psychoactive compound of the drugs listed in a list of common drugs from the US National Institute on Drug Abuse and an indication of whether these have PubChem records or acute effect estimates.

PubChem Acute Effect Estimates? (1=Yes; 0=No)	Compound	CID	URL
1	muscimol (*Amanita muscaria*)	4266	https://pubchem.ncbi.nlm.nih.gov/compound/4266#section=Acute-Effects&fullscreen=true
1	ibotenic acid (*Amanita muscaria*)	1233	https://pubchem.ncbi.nlm.nih.gov/compound/1233#section=Acute-Effects&fullscreen=true
1	ethanol (Alcohol)	702	https://pubchem.ncbi.nlm.nih.gov/compound/702#section=Acute-Effects&fullscreen=true
1	N,N-Dimethyltryptamine (Ayahuasca)	6089	https://pubchem.ncbi.nlm.nih.gov/compound/6089#section=Acute-Effects&fullscreen=true
1	cannabidiol (Cannabis)	644019	https://pubchem.ncbi.nlm.nih.gov/compound/644019#section=Acute-Effects&fullscreen=true
1	delta-9-tetrahydraconnabinol (Cannabis)	16078	https://pubchem.ncbi.nlm.nih.gov/compound/16078#section=Acute-Effects&fullscreen=true
1	delta-8-tetrahydraconnabinol (Cannabis)	638026	https://pubchem.ncbi.nlm.nih.gov/compound/638026#section=Acute-Effects&fullscreen=true
1	pentobarbital (Nembutal®)	4737	https://pubchem.ncbi.nlm.nih.gov/compound/4737#section=Acute-Effects&fullscreen=true
1	alprazolam (Xanax®)	134664	https://pubchem.ncbi.nlm.nih.gov/compound/134664#section=Acute-Effects&fullscreen=true
1	chlorodiazepoxide (Librium®)	2712	https://pubchem.ncbi.nlm.nih.gov/compound/2712#section=Acute-Effects&fullscreen=true
1	diazepam (Valium®)	3016	https://pubchem.ncbi.nlm.nih.gov/compound/3016#section=Acute-Effects&fullscreen=true
1	lorazepam (Ativan®)	3958	https://pubchem.ncbi.nlm.nih.gov/compound/3958#section=Acute-Effects&fullscreen=true
1	triazolam (Halicon®)	5556	https://pubchem.ncbi.nlm.nih.gov/compound/5556#section=Acute-Effects&fullscreen=true
0	eszopiclone (Lunesta®)	969472	
0	zaleplon (Sonata®)	5719	
1	zolpidem (Ambien®)	5732	https://pubchem.ncbi.nlm.nih.gov/compound/5732#section=Acute-Effects&fullscreen=true
1	cocaine (Coke/Crack)	446220	https://pubchem.ncbi.nlm.nih.gov/compound/446220#section=Acute-Effects&fullscreen=true
1	gamma-hydroxybutyrate (GHB)	10413	https://pubchem.ncbi.nlm.nih.gov/compound/10413#section=Acute-Effects&fullscreen=true
1	sodium oxybate (GHB)	23663870	https://pubchem.ncbi.nlm.nih.gov/compound/23663870#section=Acute-Effects&fullscreen=true
1	ketamine	3821	https://pubchem.ncbi.nlm.nih.gov/compound/3821#section=Acute-Effects&fullscreen=true
1	lysergic acid diethlymide (LSD)	5761	https://pubchem.ncbi.nlm.nih.gov/compound/5761#section=Acute-Effects&fullscreen=true
1	mescaline (Peyote)	4076	https://pubchem.ncbi.nlm.nih.gov/compound/4076#section=Acute-Effects&fullscreen=true
1	phencyclidine (PCP)	6468	https://pubchem.ncbi.nlm.nih.gov/compound/6468#section=Acute-Effects&fullscreen=true

1	heroin	5462328	https://pubchem.ncbi.nlm.nih.gov/compound/5462328#section=Acute-Effects&fullscreen=true
1	amyl nitrite (Inhalant)	10026	https://pubchem.ncbi.nlm.nih.gov/compound/10026#section=Acute-Effects&fullscreen=true
1	cathinone (Khat)	62258	https://pubchem.ncbi.nlm.nih.gov/compound/62258#section=Acute-Effects&fullscreen=true
0	mitragynine (Kratom)	3034396	
0	7-hydroxymitragynine (Kratom)	44301524	
0	3,4-Methylenedioxymethamphetamine (MDMA/Ecstasy/Molly)	71285	https://pubchem.ncbi.nlm.nih.gov/compound/71285#section=Acute-Effects&fullscreen=true
1	aethamphetamine (Desoxyn®)	10836	https://pubchem.ncbi.nlm.nih.gov/compound/10836#section=Acute-Effects&fullscreen=true
1	dextromethorphan (DXM)	5360696	https://pubchem.ncbi.nlm.nih.gov/compound/5360696#section=Acute-Effects&fullscreen=true
1	loperamide (Imodium®)	3955	https://pubchem.ncbi.nlm.nih.gov/compound/3955#section=Acute-Effects&fullscreen=true
1	codeine (various brand names)	5284371	https://pubchem.ncbi.nlm.nih.gov/compound/5284371#section=Acute-Effects&fullscreen=true
1	fentanyl (Actiq®, Duragesic®, Sublimaze®)	3345	https://pubchem.ncbi.nlm.nih.gov/compound/3345#section=Acute-Effects&fullscreen=true
1	dydrocodone or dihydrocodeinone (Vicodin®, Norco®, Zohydro®, and others)	5284569	https://pubchem.ncbi.nlm.nih.gov/compound/5284569#section=Acute-Effects&fullscreen=true
1	hydromorphone (Dilaudid®)	5284570	https://pubchem.ncbi.nlm.nih.gov/compound/5284570#section=Acute-Effects&fullscreen=true
1	meperidine (Demerol®)	4058	https://pubchem.ncbi.nlm.nih.gov/compound/4058#section=Acute-Effects&fullscreen=true
1	methadone (Dolophine®, Methadose®)	4095	https://pubchem.ncbi.nlm.nih.gov/compound/4095#section=Acute-Effects&fullscreen=true
1	morphine (Duramorph®, MS Contin®)	5288826	https://pubchem.ncbi.nlm.nih.gov/compound/5288826#section=Acute-Effects&fullscreen=true
1	oxycodone (OxyContin®, Percodan®, Percocet®, and others)	5284603	https://pubchem.ncbi.nlm.nih.gov/compound/5284603#section=Acute-Effects&fullscreen=true
1	oxymorphone (Opana®)	5284604	https://pubchem.ncbi.nlm.nih.gov/compound/5284604#section=Acute-Effects&fullscreen=true
1	amphetamine (Adderall®)	3007	https://pubchem.ncbi.nlm.nih.gov/compound/3007#section=Acute-Effects&fullscreen=true
1	nethylphenidate (Concerta®, Ritalin®)	4158	https://pubchem.ncbi.nlm.nih.gov/compound/4158#section=Acute-Effects&fullscreen=true
1	psylocibin (Magic Mushrooms/Shrooms)	10624	https://pubchem.ncbi.nlm.nih.gov/compound/10624#section=Acute-Effects&fullscreen=true
1	flunitrazepam (Rohypnol®)	3380	https://pubchem.ncbi.nlm.nih.gov/compound/3380#section=Acute-Effects&fullscreen=true
0	salvinorin A (Salvia)	128563	
0	nandrolone (Oxandrin®)	9904	
1	oxandrolone (Anadrol®)	5878	https://pubchem.ncbi.nlm.nih.gov/compound/5878#section=Acute-Effects&fullscreen=true

1	oxymetholone (Anadrol-50®)	5281034	https://pubchem.ncbi.nlm.nih.gov/compound/5281034#section=Acute-Effects&fullscreen=true
1	testosterone cypionate (Depo-testosterone®)	441404	https://pubchem.ncbi.nlm.nih.gov/compound/441404#section=Acute-Effects&fullscreen=true
0	JWH-018 (Synthetic cannabinoids)	10382701	
0	AM-2201 (Synthetic cannabinoids)	53393997	
0	UR-144 (Synthetic cannabinoids)	44626619	
0	XLR-11 (Synthetic cannabinoids)	57501498	
0	PB-22 (Synthetic cannabinoids)	NA	
0	5F-PB-22 (Synthetic cannabinoids)	72710774	
0	APICA (Synthetic cannabinoids)	71308155	
0	STS-135 (Synthetic cannabinoids)	57404059	
0	Methylenedioxypyrovalerone (Bath Salts/Flakka)	475720864	
1	nicotine (Tobacco)	89594	https://pubchem.ncbi.nlm.nih.gov/compound/89594#section=Acute-Effects&fullscreen=true

Appendix Table 2. PubChem records for those with LD50 values in oral mouse models for the main psychedelic compounds found in Amanita muscaria and available estimates in active compounds found in other common drugs administered in the same route and species listed in a list of common drugs by the US National Institute of Drug Abuse

CID	Compound	URL	SID	Listed Dose	Effect	reference	Std. Dose (mg/kg)
89594	nicotine (Tobacco)	https://pubchem.ncbi.nlm.nih.gov/compound/89594#section=Acute-Effects&fullscreen=true	134971645	3340 ug/kg	BEHAVIORAL: TREMOR; BEHAVIORAL: MUSCLE CONTRACTION OR SPASTICITY); LUNGS, THORAX, OR RESPIRATION: DYSPNEA	Hygiene and Sanitation, 34(4-6)(187), 1969	3.34
3007	amphetamine (Adderall®)	https://pubchem.ncbi.nlm.nih.gov/compound/3007#section=Acute-Effects&fullscreen=true	134975445	21 mg/kg	NULL	Arzneimittel-Forschung. Drug Research., 23(810), 1973 [PMID:4740767]	21
4266	muscimol (*Amanita muscaria*)	https://pubchem.ncbi.nlm.nih.gov/compound/4266#section=Acute-Effects&fullscreen=true	134982431	22 mg/kg	NULL	European Patent Application., #0000338	22
1233	ibotenic acid (*Amanita muscaria*)	https://pubchem.ncbi.nlm.nih.gov/compound/1233#section=Acute-Effects&fullscreen=true	134982726	38 mg/kg	BEHAVIORAL: CHANGES IN MOTOR ACTIVITY (SPECIFIC ASSAY)	Arzneimittel-Forschung. Drug Research., 18(311), 1968 [PMID:5696006]	38
3016	diazepam (Valium®)	https://pubchem.ncbi.nlm.nih.gov/compound/3016#section=Acute-Effects&fullscreen=true	134974836	48 mg/kg	NULL	Pharmaceutical Chemistry Journal, 17(30), 1983	48
4095	methadone (Dolophine®, Methadose®)	https://pubchem.ncbi.nlm.nih.gov/compound/4095#section=Acute-Effects&fullscreen=true	134971987	70 mg/kg	NULL	Archives Internationales de Pharmacodynamie et de Therapie., 135(376), 1962	70
6468	phencyclidine (PCP)	https://pubchem.ncbi.nlm.nih.gov/compound/6468#section=Acute-Effects&fullscreen=true	134972150	75 mg/kg	NULL	Toxicology and Applied Pharmacology., 37(164), 1976	75
446220	cocaine (Coke/Crack)	https://pubchem.ncbi.nlm.nih.gov/compound/446220#section=Acute-Effects&fullscreen=true	134971337	99 mg/kg	BEHAVIORAL: EXCITEMENT; BEHAVIORAL: CONVULSIONS OR EFFECT ON SEIZURE THRESHOLD	Arzneimittel-Forschung. Drug Research., 16(1275), 1966 [PMID:6014909]	99
3955	loperamide (Imodium®)	https://pubchem.ncbi.nlm.nih.gov/compound/3955#section=Acute-Effects&fullscreen=true	135003537	105 mg/kg	SENSE ORGANS AND SPECIAL SENSES: PTOSIS: EYE; BEHAVIORAL: TREMOR	Pharmacological and Biochemical Properties of Drug Substances., 3(461), 1981	105
4158	nethylphenidate (Concerta®, Ritalin®)	https://pubchem.ncbi.nlm.nih.gov/compound/4158#section=Acute-Effects&fullscreen=true	134974024	150 mg/kg	NULL	Proceedings of the Society for Experimental Biology and	150

						Medicine., 139(100), 1972 [PMID:5007444]	
4737	pentobarbital (Nembutal®)	https://pubchem.ncbi.nlm.nih.gov/compound/4737#section=Acute-Effects&fullscreen=true	134971832	170 mg/kg	NULL	Journal of Pharmacology and Experimental Therapeutics., 118(139), 1956 [PMID:13368050]	170
2712	chlorodiazepoxide (Librium®)	https://pubchem.ncbi.nlm.nih.gov/compound/2712#section=Acute-Effects&fullscreen=true	134971653	200 mg/kg	NULL	United States Patent Document., #3966793	200
4058	meperidine (Demerol®)	https://pubchem.ncbi.nlm.nih.gov/compound/4058#section=Acute-Effects&fullscreen=true	134970866	200 mg/kg	NULL	Archives Internationales de Pharmacodynamie et de Therapie., 135(376), 1962	200
5360696	dextromethorphan (DXM)	https://pubchem.ncbi.nlm.nih.gov/compound/5360696#section=Acute-Effects&fullscreen=true	135269894	210 mg/kg	NULL	Journal of Pharmaceutical Sciences., 60(1523), 1971 [PMID:4399679]	210
5284371	codeine (various brand names)	https://pubchem.ncbi.nlm.nih.gov/compound/5284371#section=Acute-Effects&fullscreen=true	134971680	250 mg/kg	NULL	Medicinal Chemistry: A Series of Monographs., 5(318), 1965	250
3345	fentanyl (Actiq®, Duragesic®, Sublimaze®)	https://pubchem.ncbi.nlm.nih.gov/compound/3345#section=Acute-Effects&fullscreen=true	134974500	368 mg/kg	NULL	Toksikologicheskii Vestnik., (4)(20), 1995	368
62258	cathinone (Khat)	https://pubchem.ncbi.nlm.nih.gov/compound/62258#section=Acute-Effects&fullscreen=true	135019400	400 mg/kg	NULL	Mutation Research., 190(153), 1987 [PMID:3821773]	400
16078	delta-9-tetrahydracannabinol (Cannabis)	https://pubchem.ncbi.nlm.nih.gov/compound/16078#section=Acute-Effects&fullscreen=true	134982169	482 mg/kg	BEHAVIORAL: TREMOR; BEHAVIORAL: EXCITEMENT; GASTROINTESTINAL: HYPERMOTILITY, DIARRHEA	Proceedings of the Society for Experimental Biology and Medicine., 136(260), 1971 [PMID:5540621]	482
5288826	morphine (Duramorph®, MS Contin®)	https://pubchem.ncbi.nlm.nih.gov/compound/5288826#section=Acute-Effects&fullscreen=true	134970862	524 mg/kg	NULL	Arzneimittel-Forschung. Drug Research., 24(600), 1974 [PMID:4406862]	524
4076	mescaline (Peyote)	https://pubchem.ncbi.nlm.nih.gov/compound/4076#section=Acute-Effects&fullscreen=true	134971508	880 mg/kg	NULL	Journal of Pharmacology and Experimental Therapeutics., 131(115), 1961 [PMID:13708274]	880
5556	triazolam (Halicon®)	https://pubchem.ncbi.nlm.nih.gov/compound/5556#section=Acute-Effects&fullscreen=true	134996744	1080 mg/kg	BEHAVIORAL: SOMNOLENCE (GENERAL DEPRESSED ACTIVITY); AUTONOMIC NERVOUS	Cesko-Slovenska Farmacie., 37(443), 1988 [PMID:3245968]	1080

					SYSTEM: SMOOTH MUSCLE RELAXANT (MECHANISM UNDEFINED, SPASMOLYTIC)		
3380	flunitrazepam (Rohypnol®)	https://pubchem.ncbi.nlm.nih.gov/compound/3380#section=Acute-Effects&fullscreen=true	134979679	1200 mg/kg	SENSE ORGANS AND SPECIAL SENSES: PTOSIS: EYE; BEHAVIORAL: SOMNOLENCE (GENERAL DEPRESSED ACTIVITY); BEHAVIORAL: CONVULSIONS OR EFFECT ON SEIZURE THRESHOLD	Kiso to Rinsho. Clinical Report., 19(1277), 1985	1200
5878	oxandrolone (Anadrol®)	https://pubchem.ncbi.nlm.nih.gov/compound/5878#section=Acute-Effects&fullscreen=true	134971185	1832 mg/kg	SENSE ORGANS AND SPECIAL SENSES: PTOSIS: EYE; BEHAVIORAL: SOMNOLENCE (GENERAL DEPRESSED ACTIVITY); BEHAVIORAL: CONVULSIONS OR EFFECT ON SEIZURE THRESHOLD	Nippon Yakurigaku Zasshi. Japanese Journal of Pharmacology., 65(418), 1969 [PMID:4186712]	1832
3958	lorazepam (Ativan®)	https://pubchem.ncbi.nlm.nih.gov/compound/3958#section=Acute-Effects&fullscreen=true	134979720	1850 mg/kg	NULL	Iyakuhin Kenkyu. Study of Medical Supplies., 8(680), 1977	1850
702	ethanol (Alcohol)	https://pubchem.ncbi.nlm.nih.gov/compound/702#section=Acute-Effects&fullscreen=true	134971966	3450 mg/kg	NULL	Gigiena i Sanitariya. For English translation, see HYSAAV., 32(3)(31), 1967	3450
10413	gamma-hydroxybutyrate (GHB)	https://pubchem.ncbi.nlm.nih.gov/compound/10413#section=Acute-Effects&fullscreen=true	134977465	4800 mg/kg	NULL	Gekkan Yakuji. Pharmaceuticals Monthly., 8(1073), 1966	4800
638026	delta-8-tetrahydracannabinol (Cannabis)	https://pubchem.ncbi.nlm.nih.gov/compound/638026#section=Acute-Effects&fullscreen=true	134988066	>2 gm/kg	NULL	Archives Internationales de Pharmacodynamie et de Therapie., 196(133), 1972	>2000

Appendix Table 3. PubChem records for those with LD50 values in oral rat models for the main psychedelic compounds found in Amanita muscaria and available estimates in active compounds found in other common drugs administered in the same route and species listed in a list of common drugs by the US National Institute of Drug Abuse

CID	Compound	URL	SID	Listed Dose	Effect	reference	Std. Dose (mg/kg)
3345	fentanyl (Actiq®, Duragesic®, Sublimaze®)	https://pubchem.ncbi.nlm.nih.gov/compound/3345#section=Acute-Effects&fullscreen=true	134974500	18 mg/kg	NULL	Journal of Pharmacy and Pharmacology., 25(929), 1973 [PMID:4150295]	18
3007	amphetamine (Adderall®)	https://pubchem.ncbi.nlm.nih.gov/compound/3007#section=Acute-Effects&fullscreen=true	134975445	30 mg/kg	NULL	Arzneimittel-Forschung. Drug Research., 23(810), 1973 [PMID:4740767]	30
4266	muscimol (*Amanita muscaria*)	https://pubchem.ncbi.nlm.nih.gov/compound/4266#section=Acute-Effects&fullscreen=true	134982431	45 mg/kg	NULL	Arzneimittel-Forschung. Drug Research., 18(311), 1968 [PMID:5696006]	45
89594	nicotine (Tobacco)	https://pubchem.ncbi.nlm.nih.gov/compound/89594#section=Acute-Effects&fullscreen=true	134971645	50 mg/kg	NULL	Farm Chemicals Handbook., -(C219), 1991	50
4095	methadone (Dolophine®, Methadose®)	https://pubchem.ncbi.nlm.nih.gov/compound/4095#section=Acute-Effects&fullscreen=true	134971987	86 mg/kg	NULL	Archives Internationales de Pharmacodynamie et de Therapie., 180(155), 1969 [PMID:5357002]	86
3955	loperamide (Imodium®)	https://pubchem.ncbi.nlm.nih.gov/compound/3955#section=Acute-Effects&fullscreen=true	135003537	98 mg/kg	NULL	Drug Development Research., 8(279), 1986	98
5360696	dextromethorphan (DXM)	https://pubchem.ncbi.nlm.nih.gov/compound/5360696#section=Acute-Effects&fullscreen=true	135269894	116 mg/kg	BEHAVIORAL: ATAXIA; SKIN AND APPENDAGES (SKIN): HAIR: OTHER; BEHAVIORAL: CONVULSIONS OR EFFECT ON SEIZURE THRESHOLD	Arzneimittel-Forschung. Drug Research., 45(1188), 1995 [PMID:8929237]	116
4737	pentobarbital (Nembutal®)	https://pubchem.ncbi.nlm.nih.gov/compound/4737#section=Acute-Effects&fullscreen=true	134971832	125 mg/kg	BEHAVIORAL: SOMNOLENCE (GENERAL DEPRESSED ACTIVITY)	Federation Proceedings, Federation of American Societies for Experimental Biology., 7(262), 1948	125
1233	ibotenic acid (*Amanita muscaria*)	https://pubchem.ncbi.nlm.nih.gov/compound/1233#section=Acute-Effects&fullscreen=true	134982726	129 mg/kg	BEHAVIORAL: CHANGES IN MOTOR ACTIVITY (SPECIFIC ASSAY)	Arzneimittel-Forschung. Drug Research., 18(311), 1968 [PMID:5696006]	129
4058	meperidine (Demerol®)	https://pubchem.ncbi.nlm.nih.gov/compound/4058#section=Acute-Effects&fullscreen=true	134970866	162 mg/kg	NULL	Archives Internationales de Pharmacodynamie et de Therapie., 180(155), 1969 [PMID:5357002]	162

3016	diazepam (Valium®)	https://pubchem.ncbi.nlm.nih.gov/compound/3016#section=Acute-Effects&fullscreen=true	134974836	249 mg/kg	NULL	Drugs in Japan, -(500), 1995	249
5288826	morphine (Duramorph®, MS Contin®)	https://pubchem.ncbi.nlm.nih.gov/compound/5288826#section=Acute-Effects&fullscreen=true	134970862	335 mg/kg	NULL	Drugs of the Future., 2(39), 1977	335
4158	nethylphenidate (Concerta®, Ritalin®)	https://pubchem.ncbi.nlm.nih.gov/compound/4158#section=Acute-Effects&fullscreen=true	134974024	367 mg/kg	NULL	Psychopharmacology Service Center, Bulletin., 2(17), 1963	367
2712	chlorodiazepoxide (Librium®)	https://pubchem.ncbi.nlm.nih.gov/compound/2712#section=Acute-Effects&fullscreen=true	134971653	392 mg/kg	NULL	United States Patent Document., #3794726	392
3380	flunitrazepam (Rohypnol®)	https://pubchem.ncbi.nlm.nih.gov/compound/3380#section=Acute-Effects&fullscreen=true	134979679	415 mg/kg	SENSE ORGANS AND SPECIAL SENSES: PTOSIS: EYE; BEHAVIORAL: SOMNOLENCE (GENERAL DEPRESSED ACTIVITY); BEHAVIORAL: CONVULSIONS OR EFFECT ON SEIZURE THRESHOLD	Kiso to Rinsho. Clinical Report., 19(1277), 1985	415
5284371	codeine (various brand names)	https://pubchem.ncbi.nlm.nih.gov/compound/5284371#section=Acute-Effects&fullscreen=true	134971680	427 mg/kg	GASTROINTESTINAL: DECREASED MOTILITY OR CONSTIPATION	Journal of Medicinal Chemistry., 16(782), 1973	427
16078	delta-9-tetrahydracannabinol (Cannabis)	https://pubchem.ncbi.nlm.nih.gov/compound/16078#section=Acute-Effects&fullscreen=true	134982169	666 mg/kg	BEHAVIORAL: TREMOR; BEHAVIORAL: EXCITEMENT; GASTROINTESTINAL: HYPERMOTILITY, DIARRHEA	Proceedings of the Society for Experimental Biology and Medicine., 136(260), 1971 [PMID:5540621]	666
638026	delta-8-tetrahydracannabinol (Cannabis)	https://pubchem.ncbi.nlm.nih.gov/compound/638026#section=Acute-Effects&fullscreen=true	134988066	860 mg/kg	BEHAVIORAL: SOMNOLENCE (GENERAL DEPRESSED ACTIVITY); LUNGS, THORAX, OR RESPIRATION: RESPIRATORY DEPRESSION	Toxicology and Applied Pharmacology., 25(363), 1973 [PMID:4199474]	860
3958	lorazepam (Ativan®)	https://pubchem.ncbi.nlm.nih.gov/compound/3958#section=Acute-Effects&fullscreen=true	134979720	4500 mg/kg	NULL	Iyakuhin Kenkyu. Study of Medical Supplies., 8(680), 1977	4500
702	ethanol (Alcohol)	https://pubchem.ncbi.nlm.nih.gov/compound/702#section=Acute-Effects&fullscreen=true	134971966	7060 mg/kg	LUNGS, THORAX, OR RESPIRATION: OTHER CHANGES	Toxicology and Applied Pharmacology., 16(718), 1970 [PMID:5422213]	7060

23663870	sodium oxybate (GHB)	https://pubchem.ncbi.nlm.nih.gov/compound/23663870#section=Acute-Effects&fullscreen=true	134978781	9690 mg/kg	NULL	Farmakologiya i Toksikologiya, 43(714), 1980 [PMID:7450011]	9690
5556	triazolam (Halicon®)	https://pubchem.ncbi.nlm.nih.gov/compound/5556#section=Acute-Effects&fullscreen=true	134996744	>7500 mg/kg	NULL	Yakkyoku. Pharmacy., 35(1074), 1984	>7500
5878	oxandrolone (Anadrol®)	https://pubchem.ncbi.nlm.nih.gov/compound/5878#section=Acute-Effects&fullscreen=true	134971185	>10 gm/kg	NULL	Nippon Yakurigaku Zasshi. Japanese Journal of Pharmacology., 65(418), 1969 [PMID:4186712]	>10000