IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Patent Assignee	Confirmation No.:
Serial No.:	##/###,###	Group No.:
Filing or 371(c) Date:	Month Day, Year	Examiner:

Entitled: Title of patent application of the client's choice for third party intervention

THIRD-PARTY PRE-ISSUANCE SUBMISSION

Examiner:

The following documents, which are also identified in the Form PTO/SB/429 filed herewith, are submitted for your consideration as being of potential relevance to the examination of the present application:

1. CHILTON (1979) "Psilocin, Bufotenine and Serotonin: Historical and Biosynthetic Observations" Journal of Psychedelic Drugs. 11(1-2).
2. FOZARD (1978) "Dual mechanism of the stimulant action of N,N-dimethyl-5-hydroxytryptamine (bufotenine) on cardiac sympathetic nerves" European Journal of Pharmacology. 49(1):25-30.
3. SHULGIN (1997) Tihkal: Tryptamines I Have Known And Loved: The Chemistry Continues. Transform Press ISBN:0-9630096-9-9.
4. OTT (1999) "Human Pharmacology of Oral DMT Plus Harmine" Journal of Psychoactive Drugs. 31(2):171-177.
5. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469.
6. BARRETT (2006) "Patterns of simultaneous polysubstance use in drug using university students" Hum. Psychopharmacol. Clin. Exp. 21: 255–263.
7. LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363.
8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46.
9. SCHECHTER (1998) "'Candyflipping': Synergistic discriminative effect of LSD and MDMA" European Journal of Pharmacology. 314: 131-134.

Attached hereto is a claim chart providing a concise description of the relevance of each reference in the document list to the elements of the presently pending claims.

U.S.S.N. ##/###,### Pending Claims	References
1. A composition comprising a combination of first serotonergic drug and a second serotonergic drug.	5. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469. From p. **465** **Table IV.** *Combined functional substance use reported by the sample over the past year* Used with [substance] to improve its effects cannabis (n = 153): – / amphetamines (n = 60): 16 / ecstasy (n = 43): 18 / LSD (n = 17): 8 / cocaine (n = 44): 14 / alcohol (n = 128): 93 amphetamines: 37 / – / 20 / 7 / 3 / 29 ecstasy: 55 / 39 / – / 11 / 19 / 45 LSD: 24 / 10 / 9 / – / 3 / 6 cocaine: 42 / 4 / 5 / 1 / – / 45 alcohol: 110 / 38 / 23 / 4 / 29 / – hallucinogenic mushrooms: 2 / 0 / 0 / 1 / 0 / 1 Used to help ease after effects of [substance] cannabis (n = 223): – / amphetamines (n = 19): 5 / ecstasy (n = 15): 2 / LSD (n = 3): 0 / cocaine (n = 23): 4 / alcohol (n = 112): 18 amphetamines: 83 / – / 6 / 1 / 1 / 47 ecstasy: 114 / 7 / – / 3 / 10 / 59 LSD: 29 / 0 / 5 / – / 0 / 13 cocaine: 80 / 1 / 1 / 0 / – / 34 alcohol: 70 / 18 / 7 / 0 / 14 / –
2. The composition of claim 1, wherein the first serotonergic drug is a psilocybin derivative.	1. CHILTON (1979) "Psilocin, Bufotenine and Serotonin: Historical and Biosynthetic Observations" Journal of Psychedelic Drugs. 11(1-2). From **p. 66** "If such a tryptophan-epoxide could be prepared in the laboratory, it would be expected to have only a very short lifetime, opening spontaneously to either 4-hydroxytryptophan, a potential precursor to the **4-hydroxytryptamine series (psilocin, psilocybin, baeocystin)** or to the 5-hydroxy series, serotonin and bufotenine...**The question is particularly pertinent for those species and genera which produce both 4-hydroxy- and 5-hydroxytryptamines together**" 7. LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363. From **p. 352** "SPU was prevalent among MDMA, D-lysergic acid diethylamide (LSD), and **psilocybin** users, in particular with alcohol and cannabis. Among MDMA users, 69% had combined MDMA with amphetamines, 56% with hallucinogens, and 47% with cocaine." From **p. 356**

	Table 2. Lifetime history of simultaneous substance use MDMA (%) / Psilocybin (%) / LSD (%) Combined with — Rarely / Often / Always Alcohol 16 28 52 10 33 21 12 33 34 Cannabis 20 32 30 17 34 30 16 28 34 Amphetamines 31 26 12 15 6 7 18 6 7 MDMA — — — 21 9 1 31 15 6 Cocaine 34 12 1 14 5 0 13 4 1 Psilocybin 18 10 0 — — — 18 6 1 Inhalants 11 5 0 9 1 1 16 3 0 LSD 32 9 1 15 6 0 — — — Opioids 3 5 2 1 1 0 7 3 0 Benzodiazepines 9 6 0 3 5 0 7 0 0 Phenethylamines[a] 24 1 1 10 1 0 21 1 0 Ketamine 18 3 0 7 1 1 13 3 0 GHB 18 5 0 8 2 0 13 4 0 MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid. [a]Phenethylamines: 2C-B, 2C-E, 2C-I, 2C-T-4, 2C-T-7. Values shown are percentages of MDMA ($n = 93$), psilocybin ($n = 86$), or LSD ($n = 67$) users combining at different frequencies with each of the compounds listed on the left. Frequency categories: "rarely" (<10%), "often" (~50%), and "always" (>90%). Each user may be counted in more than one substance category. From **p. 356** Table 3. Substance co-administration at last recalled administration of each substance Any / Alcohol / Cannabis / Amphetamines / MDMA / Cocaine / Other Cannabis (98) 62 (52–71) 52 (42–62) — 5 (2–12) 7 (3–14) 3 (1–9) 22 (15–32) Amphetamines (93) 90 (82–95) 84 (75–91) 35 (27–46) — 13 (7–21) 10 (5–18) 25 (17–34) MDMA (93) 92 (85–97) 77 (68–85) 49 (40–59) 23 (15–32) — 17 (11–26) 39 (29–49) Cocaine (91) 97 (90–99) 87 (78–92) 40 (30–50) 13 (8–22) 14 (8–23) — 21 (14–30) Psilocybin (86) 69 (58–77) 44 (34–55) 44 (34–55) 10 (5–19) 9 (5–18) 2 (0–9) 24 (17–35) Inhalants (77) 75 (65–84) 53 (42–64) 23 (15–34) 6 (2–15) 13 (7–22) 4 (1–11) 30 (21–41) LSD (67) 90 (80–95) 63 (51–73) 46 (35–58) 10 (5–20) 16 (9–27) 6 (2–15) 40 (29–52) Opioids (60) 60 (47–71) 38 (27–51) 33 (23–46) 5 (1–14) 7 (2–16) 3 (0–12) 8 (3–18) Benzodiazepines (57) 81 (68–89) 47 (35–60) 35 (24–48) 23 (14–35) 14 (7–26) 9 (3–19) 18 (10–30) GHB (49) 65 (51–77) 35 (23–49) 33 (21–47) 12 (5–25) 6 (1–17) 8 (3–20) 14 (7–27) Ketamine (49) 82 (68–90) 59 (45–72) 43 (30–57) 12 (5–25) 12 (5–25) 10 (4–22) 39 (26–53) MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid. Percentages of users of each substance in the left column reporting co-administration with any substance (excluding tobacco), alcohol, cannabis, amphetamines, MDMA, cocaine, or other substances at the last recalled use. 95% confidence intervals are given in parentheses. The number of user reports for each substance is given in parentheses in the left column. Each substance user may be counted in more than one substance category.
3. The composition of claim 1, wherein the first serotonergic drug is chosen from;	
(a) N,N-Dimethyl-5-hydroxy-T;	1. CHILTON (1979) "Psilocin, Bufotenine and Serotonin: Historical and Biosynthetic Observations" Journal of Psychedelic Drugs. 11(1-2). From **p. 66** "If such a tryptophan-epoxide could be prepared in the laboratory, it would be expected to have only a very short lifetime, opening spontaneously to either 4-hydroxytryptophan, a potential precursor to the 4-hydroxytryptamine series (psilocin, psilocybin, baeocystin) or to the **5-hydroxy series, serotonin and bufotenine...The question is particularly pertinent for those species and genera which produce both 4-hydroxy- and 5-hydroxytryptamines together.**" 2. FOZARD (1978) "Dual mechanism of the stimulant action of N,N-dimethyl-5-hydroxytryptamine (bufotenine) on cardiac sympathetic nerves" European Journal of Pharmacology. 49(1):25-30. From **p. 25** "**N,N-Dimethyl-5-hydroxytryptamine (bufotenine)** is a potent stimulant of tryptamine receptors on a variety of smooth muscle (Vane, 1959; Barlow and Khan, 1959; Bertaccini and Zamboni, 1961) and nervous (Gyermek and Bindler, 1962; Haefely, 1974a) preparations." 4. OTT (1999) "Human Pharmacology of Oral DMT Plus Harmine" Journal of Psychoactive Drugs. 31(2):171-177.

	From **p.171** "However, a paricá snuff of the Piaroa Indians of the Venezuelan Orinoco region contained tryptamines--**5-OH-DMT [bufotenine]**, DMT and 5MeO-DMT -together with the ß-carboline alkaloid harmine."
(b) alpha-Methyl-T;	1. CHILTON (1979) "Psilocin, Bufotenine and Serotonin: Historical and Biosynthetic Observations" Journal of Psychedelic Drugs. 11(1-2). From **p. 66** "Using the miniculture technique we found that a wide range of tryptamines, including the unnatural substrates diethyltryptamine (DET) and **alpha-methyl-tryptamine (AMT),** were readily absorbed by the mycelia and translocated into developing mushrooms. 8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46. From **p.28** "**Alpha-methyltryptamine (AMT)** was firstly developed as an **antidepressant agent** called as INDOPAN, in 1960's by the Upjohn Company and used for a short period of time in the former Soviet Union [20], but at last it was recognized as a toxic substance able to produce psychosis [21]. AMT activity is linked with the release of dopamine and its re-uptake inhibition. **AMT also acts on serotonin** and noradrenaline receptors and inhibits MAO activity in vitro and in vivo, therefore it is active after oral administration."
(c) N,N-Diethyl-T;	1. CHILTON (1979) "Psilocin, Bufotenine and Serotonin: Historical and Biosynthetic Observations" Journal of Psychedelic Drugs. 11(1-2). From **p. 66** "Using the miniculture technique we found that a wide range of tryptamines, including the unnatural substrates **diethyltryptamine (DET)** and alpha-methyl-tryptamine (AMT**),** were readily absorbed by the mycelia and translocated into developing mushrooms."
(d) N,N-Dimethyl-T;	1. CHILTON (1979) "Psilocin, Bufotenine and Serotonin: Historical and Biosynthetic Observations" Journal of Psychedelic Drugs. 11(1-2). From **p. 66** "We noted that deuterated tryptamine was incorporated more efficiently into psilocin and psilocybin than were monomethyltryptamine (MMT) or **dimethyltryptamine (DMT)**. Both of the latter two were incorporated, however, without prior demethylation to tryptamine." 3. SHULGIN (1997) Tihkal: Tryptamines I Have Known And Loved: The Chemistry Continues. Transform Press ISBN:0-9630096-9-9. From **48_tryptamines line. 256** "**DMT and 5-MeO-DMT are the mainstay chemicals in most snuffs, and can be introduced into the product from any of several plants**" From **48_tryptamines line. 261** "With several of the experimental subjects in this study, the **DMT was preceded by the administration of 1-methyl-**

	d-lysergic acid butanolamide (UML-491), a potent serotonin antagonist." 4. OTT (1999) "Human Pharmacology of Oral DMT Plus Harmine" Journal of Psychoactive Drugs. 31(2):171-177. From **p. 171** "A summary is presented of human self-experiments or psychonautic bioassays of pharmahuasca - capsules containing crystalline **N,N-dimethyltryptamine (DMT) plus harmine, as well as combinations of other psychoactive tryptamines with other ß-carbolines.**" From **p.171** "A 1967 analysis of a half-dozen South American snuffs used in shamanic healing by the Tucano, Waiká , Araraibo, Piaroa and Surára Indians, showed all but one of the powders to contain tryptamines, mainly **5-methoxy-N,N-dimethyltryptamine [5-MeO-DMT] and secondarily N,N-dimethyltryptamine [DMT]** (HOLMSTEDT & LINDGREN 1967). However, a paricá snuff of the Piaroa Indians of the Venezuelan Orinoco region contained tryptamines--5-OH-DMT [bufotenine], **DMT** and 5MeO-DMT -together with the ß-carboline alkaloid harmine." 8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46. From p. 29 "**DMT binds several serotonin receptors, acting as a partial agonist in particular on the 5-HT2A and 5-HT2C receptors.**" From **p. 40** ""An unidentified peak was detected in both the blood and urine specimen on the alkaline drug screen: subsequent mass spectral analysis identified the substance as **5-MeO-DMT**". In the heart blood sample was identified **N,N-dimethyltryptamine** (0.02 mg/L), 5-methoxy N,Ndimethyltryptamine (1.88 mg/L), tetrahydroharmine (0.38 mg/L), harmaline (0.07 mg/L), and harmine (0.17 mg/L)."
(e) 5-Methyoxy-alpha-methyl-T	8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46. From **p. 28** "Furthermore, he discovered that **5-MeO-AMT**, "inhibited monoamine (dopamine, 5-HT and norepinephrine) re-uptake and stimulated monoamine release; its potency was second to that of AMT."
(f) alpha-Ethyl-T	8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46. From **p.29** "Also **alpha-ethyltryptamine (AET)** was firstly introduced as **an antidepressant agent** by Upjohn company in 1960s with the name MONASE, but it was withdrawn from the market because of an unacceptable incidence of idiosyncratic agranulocytosis. AET may induce serotonin neurotoxicity [26]"
(g) N-Dimethyl-T	8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46.

	From p. 29 "Further, tryptamine undergoes a methylation process, generating the intermediate product **N-methyltryptamine (NMT). NMT is in turn transmethylated to form the final product N,N-dimethyl tryptamine.**"
(h) N,N-Diethyl-T	8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46. From **p.29** "Its mechanism of action is not clear, but, like other psychedelic tryptamines, **DET** could present an agonist activity towards serotonin receptors [31, 32]."
(i) N,N-Dipropyl-T	8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46. From **p.29** "There are few peer-reviewed experimental studies that try to explain the ways of interaction among **DPT** and serotonin receptors: Nagai revealed a strong inhibition of 5-HT reuptake in rat synaptosomes [16], and Thiagaraj also observed a moderate affinity partial agonism at the human 5-HT1A receptor [34]."
(j) N,N-Diisopropyl-T	8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46. From **p.29** "**Diisopropyl-tryptamine (DiPT)**...It is an agonist at 5HT2A receptors and a partial agonist at 5HT1A receptors [37], but 5-HT1A activity "is not thought to be necessary for hallucinogenic effects" [38]. Furthermore, DiPT blocks the serotonin uptake and it has little interaction with dopamine or norepinephrine transporters [16]."
(k) 5-Methoxy-N,N-dimethyl-T	8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46. From **p.31** "P.31 "**5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**...it has high affinity for the 5-HT1A serotonin receptor"" From **p.38** "He purchased on the Internet some Syrian rue seeds containing harmaline, a natural MAOI [76]. After ingestion of seeds, smoking 10 mg of **5-MeO-DMT**, and insufflation of further 15-20 mg, his friends found him collapsed, agitated and hallucinating. He arrived in E.D. with tachycardia (heart rate 186 bpm) and hyperpyrexia (40.7°C). He required physical restraint and clinicians administered to him 2.5 mg of IV **lorazepam**." From **p. 40** ""An unidentified peak was detected in both the blood and urine specimen on the alkaline drug screen: subsequent mass spectral analysis identified the substance as **5-MeO-DMT**". In the heart blood sample was identified N,N-dimethyltryptamine (0.02 mg/L), **5-methoxy N,Ndimethyltryptamine** (1.88 mg/L), tetrahydroharmine (0.38 mg/L), harmaline (0.07 mg/L), and harmine (0.17 mg/L)."

4. The composition of claim 1, wherein the first serotonergic drug is chosen from;	
(a) a cannabinoid	5. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469. From p. **465** **Table IV.** *Combined functional substance use reported by the sample over the past year*

	Cannabis (n = 153)	Amphetamines (n = 60)	Ecstasy (n = 43)	LSD (n = 17)	Cocaine (n = 44)	Alcohol (n = 128)
Used with [substance] to improve its effects						
cannabis	–	16	18	8	14	93
amphetamines	37	–	20	7	3	29
ecstasy	55	39	–	11	19	45
LSD	24	10	9	–	3	6
cocaine	42	4	5	1	–	45
alcohol	110	38	23	4	29	–
hallucinogenic mushrooms	2	0	0	1	0	1

	Cannabis (n = 223)	Amphetamines (n = 19)	Ecstasy (n = 15)	LSD (n = 3)	Cocaine (n = 23)	Alcohol (n = 112)
Used to help ease after effects of [substance]						
cannabis	–	5	2	0	4	18
amphetamines	83	–	6	1	1	47
ecstasy	114	7	–	3	10	59
LSD	29	0	5	–	0	13
cocaine	80	1	1	0	–	34
alcohol	70	18	7	0	14	–

6. BARRETT (2006) "Patterns of simultaneous polysubstance use in drug using university students" Hum. Psychopharmacol. Clin. Exp. 21: 255–263.

From **p. 258**

Table 2. Simultaneous polysubstance use during most recent recalled administration of each drug

Substance	Alcohol (%)	Cannabis (%)	Tobacco (%)	Alcohol, tobacco and /or cannabis (%)	Other drug(s) (%)	None (%)
Alcohol	XXX	28.2	46.9	55.1	5.3	44.9
Cannabis	37.6	XXX	47.9	65.7	2.0	32.9
Psilocybin	41.2	59.8	61.9	85.6	5.6	9.3
Ecstasy	42.7	27.6	64.0	81.3	20.0	16.0
Cocaine	79.7	40.0	77.0	95.3	7.8	4.7
Amphetamine	41.5	44.9	66.7	83.3	20.4	13.0
LSD	25.0	40.5	69.8	78.6	18.1	13.6
Methylphenidate	35.7	28.2	56.8	66.7	7.1	28.2
Ephedrine	40.7	26.1	65.2	81.5	11.1	18.5
Ketamine	38.3	33.3	83.3	88.9	33.3	5.6
GHB	40.0	26.7	46.7	73.3	26.7	20.0
Mescaline	46.6	60.0	53.3	80.0	20.0	20.0

7. LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363.

From **p.359** "Focusing on functional causes, in the present study, seven participants stated that **cannabis** enhanced (intensified or augmented) the effects of MDMA, which is in line with a previous study where 36% of cannabis users used cannabis to "improve the effects" of ecstasy (Boys et al., 2001)."

	From **p. 356** Table 2. Lifetime history of simultaneous substance use MDMA (%) / Psilocybin (%) / LSD (%) Combined with — Rarely / Often / Always Alcohol 16 28 52 10 33 21 12 33 34 Cannabis 20 32 30 17 34 30 16 28 34 Amphetamines 31 26 12 15 6 7 18 6 7 MDMA — — — 21 9 1 31 15 6 Cocaine 34 12 1 14 5 0 13 4 1 Psilocybin 18 10 0 — — — 18 6 1 Inhalants 11 5 0 9 1 1 16 3 0 LSD 32 9 1 15 6 0 — — — Opioids 3 5 2 1 1 0 7 3 0 Benzodiazepines 9 6 0 3 5 0 7 0 0 Phenethylamines[a] 24 1 1 10 1 0 21 1 0 Ketamine 18 3 0 7 1 1 13 3 0 GHB 18 5 0 8 2 0 13 4 0 MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid. [a]Phenethylamines: 2C-B, 2C-E, 2C-I, 2C-T-4, 2C-T-7. Values shown are percentages of MDMA ($n = 93$), psilocybin ($n = 86$), or LSD ($n = 67$) users combining at different frequencies with each of the compounds listed on the left. Frequency categories: "rarely" (<10%), "often" (~50%), and "always" (>90%). Each user may be counted in more than one substance category. From **p. 356** Table 3. Substance co-administration at last recalled administration of each substance Any / Alcohol / Cannabis / Amphetamines / MDMA / Cocaine / Other Cannabis (98) 62 (52–71) 52 (42–62) — 5 (2–12) 7 (3–14) 3 (1–9) 22 (15–32) Amphetamines (93) 90 (82–95) 84 (75–91) 35 (27–46) — 13 (7–21) 10 (5–18) 25 (17–34) MDMA (93) 92 (85–97) 77 (68–85) 49 (40–59) 23 (15–32) — 17 (11–26) 39 (29–49) Cocaine (91) 97 (90–99) 87 (78–92) 40 (30–50) 13 (8–22) 14 (8–23) — 21 (14–30) Psilocybin (86) 69 (58–77) 44 (34–55) 44 (34–55) 10 (5–19) 9 (5–18) 2 (0–9) 24 (17–35) Inhalants (77) 75 (65–84) 53 (42–64) 23 (15–34) 6 (2–15) 13 (7–22) 4 (1–11) 30 (21–41) LSD (67) 90 (80–95) 63 (51–73) 46 (35–58) 10 (5–20) 16 (9–27) 6 (2–15) 40 (29–52) Opioids (60) 60 (47–71) 38 (27–51) 33 (23–46) 5 (1–14) 7 (2–16) 3 (0–12) 8 (3–18) Benzodiazepines (57) 81 (68–89) 47 (35–60) 35 (24–48) 23 (14–35) 14 (7–26) 9 (3–19) 18 (10–30) GHB (49) 65 (51–77) 35 (23–49) 33 (21–47) 12 (5–25) 6 (1–17) 8 (3–20) 14 (7–27) Ketamine (49) 82 (68–90) 59 (45–72) 43 (30–57) 12 (5–25) 12 (5–25) 10 (4–22) 39 (26–53) MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid. Percentages of users of each substance in the left column reporting co-administration with any substance (excluding tobacco), alcohol, cannabis, amphetamines, MDMA, cocaine, or other substances at the last recalled use. 95% confidence intervals are given in parentheses. The number of user reports for each substance is given in parentheses in the left column. Each substance user may be counted in more than one substance category. 10. WHITE, "Mixing DXM and Other Drugs" 2015; retrieved from Web Archive, Erowid. https://web.archive.org/web/20150422070624/https://www.erowid.org/chemicals/dxm/faq/dxm_mixing.shtml, retrieved April 22, 2015 "**DXM and cannabis is a frequent combination**, which most people seem to enjoy, at least at lower doses of DXM. High doses of DXM (third plateau and up) mixed with cannabis can be very, very dissociative and sometimes unpleasant. A few people have reported that cannabis with DXM makes them feel very stupid."
(b) lysergic acid diethylamide	5. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469. From p. **465**

Table IV. *Combined functional substance use reported by the sample over the past year*

	Cannabis (n = 153)	Amphetamines (n = 60)	Ecstasy (n = 43)	LSD (n = 17)	Cocaine (n = 44)	Alcohol (n = 128)
Used with [substance] to improve its effects						
cannabis	–	16	18	8	14	93
amphetamines	37	–	20	7	3	29
ecstasy	55	39	–	11	19	45
LSD	24	10	9	–	3	6
cocaine	42	4	5	1	–	45
alcohol	110	38	23	4	29	–
hallucinogenic mushrooms	2	0	0	1	0	1
	Cannabis (n = 223)	Amphetamines (n = 19)	Ecstasy (n = 15)	LSD (n = 3)	Cocaine (n = 23)	Alcohol (n = 112)
Used to help ease after effects of [substance]						
cannabis	–	5	2	0	4	18
amphetamines	83	–	6	1	1	47
ecstasy	114	7	–	3	10	59
LSD	29	0	5	–	0	13
cocaine	80	1	1	0	–	34
alcohol	70	18	7	0	14	–

6. BARRETT (2006) “Patterns of simultaneous polysubstance use in drug using university students” Hum. Psychopharmacol. Clin. Exp. 21: 255–263.

From **p. 258**

Table 2. Simultaneous polysubstance use during most recent recalled administration of each drug

Substance	Alcohol (%)	Cannabis (%)	Tobacco (%)	Alcohol, tobacco and /or cannabis (%)	Other drug(s) (%)	None (%)
Alcohol	XXX	28.2	46.9	55.1	5.3	44.9
Cannabis	37.6	XXX	47.9	65.7	2.0	32.9
Psilocybin	41.2	59.8	61.9	85.6	5.6	9.3
Ecstasy	42.7	27.6	64.0	81.3	20.0	16.0
Cocaine	79.7	40.0	77.0	95.3	7.8	4.7
Amphetamine	41.5	44.9	66.7	83.3	20.4	13.0
LSD	25.0	40.5	69.8	78.6	18.1	13.6
Methylphenidate	35.7	28.2	56.8	66.7	7.1	28.2
Ephedrine	40.7	26.1	65.2	81.5	11.1	18.5
Ketamine	38.3	33.3	83.3	88.9	33.3	5.6
GHB	40.0	26.7	46.7	73.3	26.7	20.0
Mescaline	46.6	60.0	53.3	80.0	20.0	20.0

7. LICHT (2012) “Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases” Hum. Psychopharmacol. Clin. Exp. 27: 352–363.

From **p. 356**

Table 2. Lifetime history of simultaneous substance use

	MDMA (%)			Psilocybin (%)			LSD (%)		
Combined with	Rarely	Often	Always	Rarely	Often	Always	Rarely	Often	Always
Alcohol	16	28	52	10	33	21	12	33	34
Cannabis	20	32	30	17	34	30	16	28	34
Amphetamines	31	26	12	15	6	7	18	6	7
MDMA	—	—	—	21	9	1	31	15	6
Cocaine	34	12	1	14	5	0	13	4	1
Psilocybin	18	10	0	—	—	—	18	6	1
Inhalants	11	5	0	9	1	1	16	3	0
LSD	32	9	1	15	6	0	—	—	—
Opioids	3	5	2	1	1	0	7	3	0
Benzodiazepines	9	6	0	3	5	0	7	0	0
Phenethylamines[a]	24	1	1	10	1	0	21	1	0
Ketamine	18	3	0	7	1	1	13	3	0
GHB	18	5	0	8	2	0	13	4	0

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
[a]Phenethylamines: 2C-B, 2C-E, 2C-I, 2C-T-4, 2C-T-7. Values shown are percentages of MDMA (n = 93), psilocybin (n = 86), or LSD (n = 67) users combining at different frequencies with each of the compounds listed on the left. Frequency categories: “rarely” (<10%), “often” (~50%), and “always” (>90%). Each user may be counted in more than one substance category.

From **p. 356**

Table 3. Substance co-administration at last recalled administration of each substance

	Any	Alcohol	Cannabis	Amphetamines	MDMA	Cocaine	Other
Cannabis (98)	62 (52–71)	52 (42–62)	—	5 (2–12)	7 (3–14)	3 (1–9)	22 (15–32)
Amphetamines (93)	90 (82–95)	84 (75–91)	35 (27–46)	—	13 (7–21)	10 (5–18)	25 (17–34)
MDMA (93)	92 (85–97)	77 (68–85)	49 (40–59)	23 (15–32)	—	17 (11–26)	39 (29–49)
Cocaine (91)	97 (90–99)	87 (78–92)	40 (30–50)	13 (8–22)	14 (8–23)	—	21 (14–30)
Psilocybin (86)	69 (58–77)	44 (34–55)	44 (34–55)	10 (5–19)	9 (5–18)	2 (0–9)	24 (17–35)
Inhalants (77)	75 (65–84)	53 (42–64)	23 (15–34)	6 (2–15)	13 (7–22)	4 (1–11)	30 (21–41)
LSD (67)	90 (80–95)	63 (51–73)	46 (35–58)	10 (5–20)	16 (9–27)	6 (2–15)	40 (29–52)
Opioids (60)	60 (47–71)	38 (27–51)	33 (23–46)	5 (1–14)	7 (2–16)	3 (0–12)	8 (3–18)
Benzodiazepines (57)	81 (68–89)	47 (35–60)	35 (24–48)	23 (14–35)	14 (7–26)	9 (3–19)	18 (10–30)
GHB (49)	65 (51–77)	35 (23–49)	33 (21–47)	12 (5–25)	6 (1–17)	8 (3–20)	14 (7–27)
Ketamine (49)	82 (68–90)	59 (45–72)	43 (30–57)	12 (5–25)	12 (5–25)	10 (4–22)	39 (26–53)

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
Percentages of users of each substance in the left column reporting co-administration with any substance (excluding tobacco), alcohol, cannabis, amphetamines, MDMA, cocaine, or other substances at the last recalled use. 95% confidence intervals are given in parentheses. The number of user reports for each substance is given in parentheses in the left column. Each substance user may be counted in more than one substance category.

(c) 3,4-methylenedioxymethamphetamine

5. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469.

From p. **465**

Table IV. *Combined functional substance use reported by the sample over the past year*

	Cannabis (n = 153)	Amphetamines (n = 60)	Ecstasy (n = 43)	LSD (n = 17)	Cocaine (n = 44)	Alcohol (n = 128)
Used with [substance] to improve its effects						
cannabis	–	16	18	8	14	93
amphetamines	37	–	20	7	3	29
ecstasy	55	39	–	11	19	45
LSD	24	10	9	–	3	6
cocaine	42	4	5	1	–	45
alcohol	110	38	23	4	29	–
hallucinogenic mushrooms	2	0	0	1	0	1
	Cannabis (n = 223)	Amphetamines (n = 19)	Ecstasy (n = 15)	LSD (n = 3)	Cocaine (n = 23)	Alcohol (n = 112)
Used to help ease after effects of [substance]						
cannabis	–	5	2	0	4	18
amphetamines	83	–	6	1	1	47
ecstasy	114	7	–	3	10	59
LSD	29	0	5	–	0	13
cocaine	80	1	1	0	–	34
alcohol	70	18	7	0	14	–

6. BARRETT (2006) "Patterns of simultaneous polysubstance use in drug using university students" Hum. Psychopharmacol. Clin. Exp. 21: 255–263.

From **p. 258**

Table 2. Simultaneous polysubstance use during most recent recalled administration of each drug

Substance	Alcohol (%)	Cannabis (%)	Tobacco (%)	Alcohol, tobacco and /or cannabis (%)	Other drug(s) (%)	None (%)
Alcohol	XXX	28.2	46.9	55.1	5.3	44.9
Cannabis	37.6	XXX	47.9	65.7	2.0	32.9
Psilocybin	41.2	59.8	61.9	85.6	5.6	9.3
Ecstasy	42.7	27.6	64.0	81.3	20.0	16.0
Cocaine	79.7	40.0	77.0	95.3	7.8	4.7
Amphetamine	41.5	44.9	66.7	83.3	20.4	13.0
LSD	25.0	40.5	69.8	78.6	18.1	13.6
Methylphenidate	35.7	28.2	56.8	66.7	7.1	28.2
Ephedrine	40.7	26.1	65.2	81.5	11.1	18.5
Ketamine	38.3	33.3	83.3	88.9	33.3	5.6
GHB	40.0	26.7	46.7	73.3	26.7	20.0
Mescaline	46.6	60.0	53.3	80.0	20.0	20.0

7. LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363.

	From **p.359** "Focusing on functional causes, in the present study, seven participants stated that cannabis enhanced (intensified or augmented) the effects of **MDMA**, which is in line with a previous study where 36% of cannabis users used cannabis to “improve the effects” of ecstasy (Boys et al., 2001)." From **p. 356** Table 2. Lifetime history of simultaneous substance use MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid. [a]Phenethylamines: 2C-B, 2C-E, 2C-I, 2C-T-4, 2C-T-7. Values shown are percentages of MDMA ($n = 93$), psilocybin ($n = 86$), or LSD ($n = 67$) users combining at different frequencies with each of the compounds listed on the left. Frequency categories: “rarely” (<10%), “often” (~50%), and “always” (>90%). Each user may be counted in more than one substance category. From **p. 356** Table 3. Substance co-administration at last recalled administration of each substance MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid. Percentages of users of each substance in the left column reporting co-administration with any substance (excluding tobacco), alcohol, cannabis, amphetamines, MDMA, cocaine, or other substances at the last recalled use. 95% confidence intervals are given in parentheses. The number of user reports for each substance is given in parentheses in the left column. Each substance user may be counted in more than one substance category.
(d) dextromethorphan	10. WHITE, “Mixing DXM and Other Drugs” 2015; retrieved from Web Archive, Erowid. https://web.archive.org/web/20150422070624/https://www.erowid.org/chemicals/dxm/faq/dxm_mixing.shtml, retrieved April 22, 2015 “Some people have reported that combining **DXM** with a low dose of a **benzodiazepine** can prevent some of the more annoying side effects (mostly related to overstimulation, high blood pressure, and tachycardia). **Clonazepam** (Clonopin[tm]) in particular has been reported to have specific effects in combination with DXM, different from other benzodiazepines. These effects include enhanced CEV's (closed-eye visuals) and, of course, limiting or preventing sympathomimetic effects (high blood pressure and heart rate, sweating, etc.).” “Most who've tried it reported that **DXM** will potentiate other stimulants. Since DXM inhibits dopamine reuptake, combining it with a dopamine releasing agent (**amphetamine** or methamphetamine) will naturally produce a combined, synergistic effect.”

	MDMA (%)			Psilocybin (%)			LSD (%)		
Combined with	Rarely	Often	Always	Rarely	Often	Always	Rarely	Often	Always
Alcohol	16	28	52	10	33	21	12	33	34
Cannabis	20	32	30	17	34	30	16	28	34
Amphetamines	31	26	12	15	6	7	18	6	7
MDMA	—	—	—	21	9	1	31	15	6
Cocaine	34	12	1	14	5	0	13	4	1
Psilocybin	18	10	0	—	—	—	18	6	1
Inhalants	11	5	0	9	1	1	16	3	0
LSD	32	9	1	15	6	0	—	—	—
Opioids	3	5	2	1	1	0	7	3	0
Benzodiazepines	9	6	0	3	5	0	7	0	0
Phenethylamines[a]	24	1	1	10	1	0	21	1	0
Ketamine	18	3	0	7	1	1	13	3	0
GHB	18	5	0	8	2	0	13	4	0

	Any	Alcohol	Cannabis	Amphetamines	MDMA	Cocaine	Other
Cannabis (98)	62 (52–71)	52 (42–62)	—	5 (2–12)	7 (3–14)	3 (1–9)	22 (15–32)
Amphetamines (93)	90 (82–95)	84 (75–91)	35 (27–46)	—	13 (7–21)	10 (5–18)	25 (17–34)
MDMA (93)	92 (85–97)	77 (68–85)	49 (40–59)	23 (15–32)	—	17 (11–26)	39 (29–49)
Cocaine (91)	97 (90–99)	87 (78–92)	40 (30–50)	13 (8–22)	14 (8–23)	—	21 (14–30)
Psilocybin (86)	69 (58–77)	44 (34–55)	44 (34–55)	10 (5–19)	9 (5–18)	2 (0–9)	24 (17–35)
Inhalants (77)	75 (65–84)	53 (42–64)	23 (15–34)	6 (2–15)	13 (7–22)	4 (1–11)	30 (21–41)
LSD (67)	90 (80–95)	63 (51–73)	46 (35–58)	10 (5–20)	16 (9–27)	6 (2–15)	40 (29–52)
Opioids (60)	60 (47–71)	38 (27–51)	33 (23–46)	5 (1–14)	7 (2–16)	3 (0–12)	8 (3–18)
Benzodiazepines (57)	81 (68–89)	47 (35–60)	35 (24–48)	23 (14–35)	14 (7–26)	9 (3–19)	18 (10–30)
GHB (49)	65 (51–77)	35 (23–49)	33 (21–47)	12 (5–25)	6 (1–17)	8 (3–20)	14 (7–27)
Ketamine (49)	82 (68–90)	59 (45–72)	43 (30–57)	12 (5–25)	12 (5–25)	10 (4–22)	39 (26–53)

	"**DXM and cannabis is a frequent combination**, which most people seem to enjoy, at least at lower doses of DXM. High doses of DXM (third plateau and up) mixed with cannabis can be very, very dissociative and sometimes unpleasant. A few people have reported that cannabis with DXM makes them feel very stupid." "I've received a limited number (about 20) of reports of mixing **DXM with 5HT hallucinogens, primarily LSD and mushrooms**. While one person said this combination was "not recommended", most have had incredibly profound experiences. On the other hand, very few of these have said they would ever repeat the combination, as it was simply far too powerful and terrifying. One person told me that DXM helped him avoid unpleasant cognitive effects and "bad trips" he might otherwise get from LSD alone. Regular use of DXM may alter the effects of LSD due to overall increase in 5HT binding (252) and decreased 5HT2 receptor binding (212)." "have very limited data on mixing these drugs with **DXM**. One person mixed DXM and **2CB** ("bees") and had a wonderful experience"
(e) clonazepam	10. WHITE, "Mixing DXM and Other Drugs" 2015; retrieved from Web Archive, Erowid. https://web.archive.org/web/20150422070624/https://www.erowid.org/chemicals/dxm/faq/dxm_mixing.shtml, retrieved April 22, 2015 "Some people have reported that combining **DXM** with a low dose of a **benzodiazepine** can prevent some of the more annoying side effects (mostly related to overstimulation, high blood pressure, and tachycardia). **Clonazepam** (Clonopin[tm]) in particular has been reported to have specific effects in combination with DXM, different from other benzodiazepines. These effects include enhanced CEV's (closed-eye visuals) and, of course, limiting or preventing sympathomimetic effects (high blood pressure and heart rate, sweating, etc.)."
(f) amphetamine	10. WHITE, "Mixing DXM and Other Drugs" 2015; retrieved from Web Archive, Erowid. https://web.archive.org/web/20150422070624/https://www.erowid.org/chemicals/dxm/faq/dxm_mixing.shtml, retrieved April 22, 2015 "Most who've tried it reported that **DXM** will potentiate other stimulants. Since DXM inhibits dopamine reuptake, combining it with a dopamine releasing agent (**amphetamine** or methamphetamine) will naturally produce a combined, synergistic effect."
(f) lysergamide	11. U.S. Pat. No. 8,859,579 From **claim 1**: "A method for treating a disorder associated with cephalic pain wherein said disorder is trigeminal autonomic cephalagia, comprising enterally, sublingually or parenterally administering to a subject in need of such treatment a therapeutically effective amount of a substantially pure form of **lysergic acid amide (LSA**) or bromo-lysergic acid diethylamide

	(bromo-LSD) present in a composition in an amount of between about 50 μg and about 5000 μg." From **claim 4**: "The method of claim 1, **further comprising administering to the subject a second compound** which acutely relieves at least one symptom of the disorder associated with cephalic pain." From **claim 5**: "The method of claim 4, wherein **the second compound is selected from the group consisting of oxygen, a serotonin receptor agonist, an ergot derivative,** a hormone, and a local anesthetic." From **[0012]**: "The methods of the invention can further include administering to the subject a second compound which acutely relieves at least one symptom of a disorder associated with cephalic pain, e.g., administering a compound described herein in combination with a second compound. **Examples of second compounds which acutely relieve at least one symptom of a disorder associated with cephalic pain include oxygen, serotonin receptor agonists** (e.g., triptans such as sumatriptan, eletriptan, rizatriptan, frovatriptan, almotriptan, zolmitriptan, and naratriptan), ergot derivatives (e.g., dihydroergotamine, and ergotamine tartrate)," 12. SHROOMERY, "Re: LSA and Shrooms [Re: MycoKris]" 2006; retrieved from https://www.shroomery.org/forums/showflat.php/Number/6033473#6033473, retrieved September 5, 2006 From **post# 6033473**: "My favorite psychedelic to use with **mushrooms is mescaline or lsa**. Thats not because I cant find lsd, ayahuasca or any rc's either. Lsa Adds some personality, geometry an control to the mushrooms wild visuals, adds a sort of framework. They both seem to potentiate the other, not like an maoi ofcoarse, but its as if one doesnt overpower the other. They both give what the other lacks, and what they have in common is stronger. A cool experiment is to see how little you really have to take of each. You could eat 3 grams of MG's and .5 grams of mushrooms after about an hour. Most people would be VERY suprized at how serious this mix is even at such and extreemely low dose."
5. The composition of claim 4, wherein the second serotonergic drug is chosen from;	
(a) a cannabinoid	5. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469. From p. **465**

Table IV. *Combined functional substance use reported by the sample over the past year*

	Cannabis (n = 153)	Amphetamines (n = 60)	Ecstasy (n = 43)	LSD (n = 17)	Cocaine (n = 44)	Alcohol (n = 128)
Used with [substance] to improve its effects						
cannabis	–	16	18	8	14	93
amphetamines	37	–	20	7	3	29
ecstasy	55	39	–	11	19	45
LSD	24	10	9	–	3	6
cocaine	42	4	5	1	–	45
alcohol	110	38	23	4	29	–
hallucinogenic mushrooms	2	0	0	1	0	1
	Cannabis (n = 223)	Amphetamines (n = 19)	Ecstasy (n = 15)	LSD (n = 3)	Cocaine (n = 23)	Alcohol (n = 112)
Used to help ease after effects of [substance]						
cannabis	–	5	2	0	4	18
amphetamines	83	–	6	1	1	47
ecstasy	114	7	–	3	10	59
LSD	29	0	5	–	0	13
cocaine	80	1	1	0	–	34
alcohol	70	18	7	0	14	–

6. BARRETT (2006) “Patterns of simultaneous polysubstance use in drug using university students” Hum. Psychopharmacol. Clin. Exp. 21: 255–263.

From **p. 258**

Table 2. Simultaneous polysubstance use during most recent recalled administration of each drug

Substance	Alcohol (%)	Cannabis (%)	Tobacco (%)	Alcohol, tobacco and /or cannabis (%)	Other drug(s) (%)	None (%)
Alcohol	XXX	28.2	46.9	55.1	5.3	44.9
Cannabis	37.6	XXX	47.9	65.7	2.0	32.9
Psilocybin	41.2	59.8	61.9	85.6	5.6	9.3
Ecstasy	42.7	27.6	64.0	81.3	20.0	16.0
Cocaine	79.7	40.0	77.0	95.3	7.8	4.7
Amphetamine	41.5	44.9	66.7	83.3	20.4	13.0
LSD	25.0	40.5	69.8	78.6	18.1	13.6
Methylphenidate	35.7	28.2	56.8	66.7	7.1	28.2
Ephedrine	40.7	26.1	65.2	81.5	11.1	18.5
Ketamine	38.3	33.3	83.3	88.9	33.3	5.6
GHB	40.0	26.7	46.7	73.3	26.7	20.0
Mescaline	46.6	60.0	53.3	80.0	20.0	20.0

7. LICHT (2012) “Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases” Hum. Psychopharmacol. Clin. Exp. 27: 352–363.

From **p.359** "Focusing on functional causes, in the present study, seven participants stated that **cannabis** enhanced (intensified or augmented) the effects of MDMA, which is in line with a previous study where 36% of cannabis users used cannabis to “improve the effects” of ecstasy (Boys et al., 2001)."

From **p. 356**

Table 2. Lifetime history of simultaneous substance use

	MDMA (%)			Psilocybin (%)			LSD (%)		
Combined with	Rarely	Often	Always	Rarely	Often	Always	Rarely	Often	Always
Alcohol	16	28	52	10	33	21	12	33	34
Cannabis	20	32	30	17	34	30	16	28	34
Amphetamines	31	26	12	15	6	7	18	6	7
MDMA	—	—	—	21	9	1	31	15	6
Cocaine	34	12	1	14	5	0	13	4	1
Psilocybin	18	10	0	—	—	—	18	6	1
Inhalants	11	5	0	9	1	1	16	3	0
LSD	32	9	1	15	6	0	—	—	—
Opioids	3	5	2	1	1	0	7	3	0
Benzodiazepines	9	6	0	3	5	0	7	0	0
Phenethylamines[a]	24	1	1	10	1	0	21	1	0
Ketamine	18	3	0	7	1	1	13	3	0
GHB	18	5	0	8	2	0	13	4	0

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
[a]Phenethylamines: 2C-B, 2C-E, 2C-I, 2C-T-4, 2C-T-7. Values shown are percentages of MDMA ($n = 93$), psilocybin ($n = 86$), or LSD ($n = 67$) users combining at different frequencies with each of the compounds listed on the left. Frequency categories: "rarely" (<10%), "often" (~50%), and "always" (>90%). Each user may be counted in more than one substance category.

From **p. 356**

Table 3. Substance co-administration at last recalled administration of each substance

	Any	Alcohol	Cannabis	Amphetamines	MDMA	Cocaine	Other
Cannabis (98)	62 (52–71)	52 (42–62)	—	5 (2–12)	7 (3–14)	3 (1–9)	22 (15–32)
Amphetamines (93)	90 (82–95)	84 (75–91)	35 (27–46)	—	13 (7–21)	10 (5–18)	25 (17–34)
MDMA (93)	92 (85–97)	77 (68–85)	49 (40–59)	23 (15–32)	—	17 (11–26)	39 (29–49)
Cocaine (91)	97 (90–99)	87 (78–92)	40 (30–50)	13 (8–22)	14 (8–23)	—	21 (14–30)
Psilocybin (86)	69 (58–77)	44 (34–55)	44 (34–55)	10 (5–19)	9 (5–18)	2 (0–9)	24 (17–35)
Inhalants (77)	75 (65–84)	53 (42–64)	23 (15–34)	6 (2–15)	13 (7–22)	4 (1–11)	30 (21–41)
LSD (67)	90 (80–95)	63 (51–73)	46 (35–58)	10 (5–20)	16 (9–27)	6 (2–15)	40 (29–52)
Opioids (60)	60 (47–71)	38 (27–51)	33 (23–46)	5 (1–14)	7 (2–16)	3 (0–12)	8 (3–18)
Benzodiazepines (57)	81 (68–89)	47 (35–60)	35 (24–48)	23 (14–35)	14 (7–26)	9 (3–19)	18 (10–30)
GHB (49)	65 (51–77)	35 (23–49)	33 (21–47)	12 (5–25)	6 (1–17)	8 (3–20)	14 (7–27)
Ketamine (49)	82 (68–90)	59 (45–72)	43 (30–57)	12 (5–25)	12 (5–25)	10 (4–22)	39 (26–53)

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
Percentages of users of each substance in the left column reporting co-administration with any substance (excluding tobacco), alcohol, cannabis, amphetamines, MDMA, cocaine, or other substances at the last recalled use. 95% confidence intervals are given in parentheses. The number of user reports for each substance is given in parentheses in the left column. Each substance user may be counted in more than one substance category.

(b) lysergic acid diethylamide

5. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469.

From p. **465**

Table IV. *Combined functional substance use reported by the sample over the past year*

	Cannabis ($n = 153$)	Amphetamines ($n = 60$)	Ecstasy ($n = 43$)	LSD ($n = 17$)	Cocaine ($n = 44$)	Alcohol ($n = 128$)
Used with [substance] to improve its effects						
cannabis	–	16	18	8	14	93
amphetamines	37	–	20	7	3	29
ecstasy	55	39	–	11	19	45
LSD	24	10	9	–	3	6
cocaine	42	4	5	1	–	45
alcohol	110	38	23	4	29	–
hallucinogenic mushrooms	2	0	0	1	0	1
	Cannabis ($n = 223$)	Amphetamines ($n = 19$)	Ecstasy ($n = 15$)	LSD ($n = 3$)	Cocaine ($n = 23$)	Alcohol ($n = 112$)
Used to help ease after effects of [substance]						
cannabis	–	5	2	0	4	18
amphetamines	83	–	6	1	1	47
ecstasy	114	7	–	3	10	59
LSD	29	0	5	–	0	13
cocaine	80	1	1	0	–	34
alcohol	70	18	7	0	14	–

6. BARRETT (2006) "Patterns of simultaneous polysubstance use in drug using university students" Hum. Psychopharmacol. Clin. Exp. 21: 255–263.

From **p. 258**

Table 2. Simultaneous polysubstance use during most recent recalled administration of each drug

Substance	Alcohol (%)	Cannabis (%)	Tobacco (%)	Alcohol, tobacco and /or cannabis (%)	Other drug(s) (%)	None (%)
Alcohol	XXX	28.2	46.9	55.1	5.3	44.9
Cannabis	37.6	XXX	47.9	65.7	2.0	32.9
Psilocybin	41.2	59.8	61.9	85.6	5.6	9.3
Ecstasy	42.7	27.6	64.0	81.3	20.0	16.0
Cocaine	79.7	40.0	77.0	95.3	7.8	4.7
Amphetamine	41.5	44.9	66.7	83.3	20.4	13.0
LSD	25.0	40.5	69.8	78.6	18.1	13.6
Methylphenidate	35.7	28.2	56.8	66.7	7.1	28.2
Ephedrine	40.7	26.1	65.2	81.5	11.1	18.5
Ketamine	38.3	33.3	83.3	88.9	33.3	5.6
GHB	40.0	26.7	46.7	73.3	26.7	20.0
Mescaline	46.6	60.0	53.3	80.0	20.0	20.0

7. LICHT (2012) “Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases” Hum. Psychopharmacol. Clin. Exp. 27: 352–363.

From **p. 356**

Table 2. Lifetime history of simultaneous substance use

	MDMA (%)			Psilocybin (%)			LSD (%)		
Combined with	Rarely	Often	Always	Rarely	Often	Always	Rarely	Often	Always
Alcohol	16	28	52	10	33	21	12	33	34
Cannabis	20	32	30	17	34	30	16	28	34
Amphetamines	31	26	12	15	6	7	18	6	7
MDMA	—	—	—	21	9	1	31	15	6
Cocaine	34	12	1	14	5	0	13	4	1
Psilocybin	18	10	0	—	—	—	18	6	1
Inhalants	11	5	0	9	1	1	16	3	0
LSD	32	9	1	15	6	0	—	—	—
Opioids	3	5	2	1	1	0	7	3	0
Benzodiazepines	9	6	0	3	5	0	7	0	0
Phenethylamines[a]	24	1	1	10	1	0	21	1	0
Ketamine	18	3	0	7	1	1	13	3	0
GHB	18	5	0	8	2	0	13	4	0

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
[a]Phenethylamines: 2C-B, 2C-E, 2C-I, 2C-T-4, 2C-T-7. Values shown are percentages of MDMA ($n = 93$), psilocybin ($n = 86$), or LSD ($n = 67$) users combining at different frequencies with each of the compounds listed on the left. Frequency categories: “rarely” (<10%), “often” (~50%), and “always” (>90%). Each user may be counted in more than one substance category.

From **p. 356**

Table 3. Substance co-administration at last recalled administration of each substance

	Any	Alcohol	Cannabis	Amphetamines	MDMA	Cocaine	Other
Cannabis (98)	62 (52–71)	52 (42–62)	—	5 (2–12)	7 (3–14)	3 (1–9)	22 (15–32)
Amphetamines (93)	90 (82–95)	84 (75–91)	35 (27–46)	—	13 (7–21)	10 (5–18)	25 (17–34)
MDMA (93)	92 (85–97)	77 (68–85)	49 (40–59)	23 (15–32)	—	17 (11–26)	39 (29–49)
Cocaine (91)	97 (90–99)	87 (78–92)	40 (30–50)	13 (8–22)	14 (8–23)	—	21 (14–30)
Psilocybin (86)	69 (58–77)	44 (34–55)	44 (34–55)	10 (5–19)	9 (5–18)	2 (0–9)	24 (17–35)
Inhalants (77)	75 (65–84)	53 (42–64)	23 (15–34)	6 (2–15)	13 (7–22)	4 (1–11)	30 (21–41)
LSD (67)	90 (80–95)	63 (51–73)	46 (35–58)	10 (5–20)	16 (9–27)	6 (2–15)	40 (29–52)
Opioids (60)	60 (47–71)	38 (27–51)	33 (23–46)	5 (1–14)	7 (2–16)	3 (0–12)	8 (3–18)
Benzodiazepines (57)	81 (68–89)	47 (35–60)	35 (24–48)	23 (14–35)	14 (7–26)	9 (3–19)	18 (10–30)
GHB (49)	65 (51–77)	35 (23–49)	33 (21–47)	12 (5–25)	6 (1–17)	8 (3–20)	14 (7–27)
Ketamine (49)	82 (68–90)	59 (45–72)	43 (30–57)	12 (5–25)	12 (5–25)	10 (4–22)	39 (26–53)

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
Percentages of users of each substance in the left column reporting co-administration with any substance (excluding tobacco), alcohol, cannabis, amphetamines, MDMA, cocaine, or other substances at the last recalled use. 95% confidence intervals are given in parentheses. The number of user reports for each substance is given in parentheses in the left column. Each substance user may be counted in more than one substance category.

(c) 3,4-methylenedioxymethamphetamine	5. BOYS (2001) “Understanding reasons for drug use amongst young people a functional perspective” Health Education Research. 16(4):457-469. From p. **465**

Table IV. *Combined functional substance use reported by the sample over the past year*

	Cannabis (n = 153)	Amphetamines (n = 60)	Ecstasy (n = 43)	LSD (n = 17)	Cocaine (n = 44)	Alcohol (n = 128)
Used with [substance] to improve its effects						
cannabis	–	16	18	8	14	93
amphetamines	37	–	20	7	3	29
ecstasy	55	39	–	11	19	45
LSD	24	10	9	–	3	6
cocaine	42	4	5	1	–	45
alcohol	110	38	23	4	29	–
hallucinogenic mushrooms	2	0	0	1	0	1
	Cannabis (n = 223)	Amphetamines (n = 19)	Ecstasy (n = 15)	LSD (n = 3)	Cocaine (n = 23)	Alcohol (n = 112)
Used to help ease after effects of [substance]						
cannabis	–	5	2	0	4	18
amphetamines	83	–	6	1	1	47
ecstasy	114	7	–	3	10	59
LSD	29	0	5	–	0	13
cocaine	80	1	1	0	–	34
alcohol	70	18	7	0	14	–

6. BARRETT (2006) “Patterns of simultaneous polysubstance use in drug using university students” Hum. Psychopharmacol. Clin. Exp. 21: 255–263.

From **p. 258**

Table 2. Simultaneous polysubstance use during most recent recalled administration of each drug

Substance	Alcohol (%)	Cannabis (%)	Tobacco (%)	Alcohol, tobacco and /or cannabis (%)	Other drug(s) (%)	None (%)
Alcohol	XXX	28.2	46.9	55.1	5.3	44.9
Cannabis	37.6	XXX	47.9	65.7	2.0	32.9
Psilocybin	41.2	59.8	61.9	85.6	5.6	9.3
Ecstasy	42.7	27.6	64.0	81.3	20.0	16.0
Cocaine	79.7	40.0	77.0	95.3	7.8	4.7
Amphetamine	41.5	44.9	66.7	83.3	20.4	13.0
LSD	25.0	40.5	69.8	78.6	18.1	13.6
Methylphenidate	35.7	28.2	56.8	66.7	7.1	28.2
Ephedrine	40.7	26.1	65.2	81.5	11.1	18.5
Ketamine	38.3	33.3	83.3	88.9	33.3	5.6
GHB	40.0	26.7	46.7	73.3	26.7	20.0
Mescaline	46.6	60.0	53.3	80.0	20.0	20.0

7. LICHT (2012) “Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases” Hum. Psychopharmacol. Clin. Exp. 27: 352–363.

From **p.359** "Focusing on functional causes, in the present study, seven participants stated that cannabis enhanced (intensified or augmented) the effects of **MDMA**, which is in line with a previous study where 36% of cannabis users used cannabis to “improve the effects” of ecstasy (Boys et al., 2001)."

From **p. 356**

Table 2. Lifetime history of simultaneous substance use

	MDMA (%)			Psilocybin (%)			LSD (%)		
Combined with	Rarely	Often	Always	Rarely	Often	Always	Rarely	Often	Always
Alcohol	16	28	52	10	33	21	12	33	34
Cannabis	20	32	30	17	34	30	16	28	34
Amphetamines	31	26	12	15	6	7	18	6	7
MDMA	—	—	—	21	9	1	31	15	6
Cocaine	34	12	1	14	5	0	13	4	1
Psilocybin	18	10	0	—	—	—	18	6	1
Inhalants	11	5	0	9	1	1	16	3	0
LSD	32	9	1	15	6	0	—	—	—
Opioids	3	5	2	1	1	0	7	3	0
Benzodiazepines	9	6	0	3	5	0	7	0	0
Phenethylamines[a]	24	1	1	10	1	0	21	1	0
Ketamine	18	3	0	7	1	1	13	3	0
GHB	18	5	0	8	2	0	13	4	0

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
[a]Phenethylamines: 2C-B, 2C-E, 2C-I, 2C-T-4, 2C-T-7. Values shown are percentages of MDMA ($n = 93$), psilocybin ($n = 86$), or LSD ($n = 67$) users combining at different frequencies with each of the compounds listed on the left. Frequency categories: "rarely" (<10%), "often" (~50%), and "always" (>90%). Each user may be counted in more than one substance category.

From **p. 356**

Table 3. Substance co-administration at last recalled administration of each substance

	Any	Alcohol	Cannabis	Amphetamines	MDMA	Cocaine	Other
Cannabis (98)	62 (52–71)	52 (42–62)	—	5 (2–12)	7 (3–14)	3 (1–9)	22 (15–32)
Amphetamines (93)	90 (82–95)	84 (75–91)	35 (27–46)	—	13 (7–21)	10 (5–18)	25 (17–34)
MDMA (93)	92 (85–97)	77 (68–85)	49 (40–59)	23 (15–32)	—	17 (11–26)	39 (29–49)
Cocaine (91)	97 (90–99)	87 (78–92)	40 (30–50)	13 (8–22)	14 (8–23)	—	21 (14–30)
Psilocybin (86)	69 (58–77)	44 (34–55)	44 (34–55)	10 (5–19)	9 (5–18)	2 (0–9)	24 (17–35)
Inhalants (77)	75 (65–84)	53 (42–64)	23 (15–34)	6 (2–15)	13 (7–22)	4 (1–11)	30 (21–41)
LSD (67)	90 (80–95)	63 (51–73)	46 (35–58)	10 (5–20)	16 (9–27)	6 (2–15)	40 (29–52)
Opioids (60)	60 (47–71)	38 (27–51)	33 (23–46)	5 (1–14)	7 (2–16)	3 (0–12)	8 (3–18)
Benzodiazepines (57)	81 (68–89)	47 (35–60)	35 (24–48)	23 (14–35)	14 (7–26)	9 (3–19)	18 (10–30)
GHB (49)	65 (51–77)	35 (23–49)	33 (21–47)	12 (5–25)	6 (1–17)	8 (3–20)	14 (7–27)
Ketamine (49)	82 (68–90)	59 (45–72)	43 (30–57)	12 (5–25)	12 (5–25)	10 (4–22)	39 (26–53)

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
Percentages of users of each substance in the left column reporting co-administration with any substance (excluding tobacco), alcohol, cannabis, amphetamines, MDMA, cocaine, or other substances at the last recalled use. 95% confidence intervals are given in parentheses. The number of user reports for each substance is given in parentheses in the left column. Each substance user may be counted in more than one substance category.

(d) dextromethorphan

10. WHITE, "Mixing DXM and Other Drugs" 2015; retrieved from Web Archive, Erowid. https://web.archive.org/web/20150422070624/https://www.erowid.org/chemicals/dxm/faq/dxm_mixing.shtml, retrieved April 22, 2015

"Some people have reported that combining **DXM** with a low dose of a **benzodiazepine** can prevent some of the more annoying side effects (mostly related to overstimulation, high blood pressure, and tachycardia). **Clonazepam** (Clonopin[tm]) in particular has been reported to have specific effects in combination with DXM, different from other benzodiazepines. These effects include enhanced CEV's (closed-eye visuals) and, of course, limiting or preventing sympathomimetic effects (high blood pressure and heart rate, sweating, etc.)."

"Most who've tried it reported that **DXM** will potentiate other stimulants. Since DXM inhibits dopamine reuptake, combining it with a dopamine releasing agent (**amphetamine** or methamphetamine) will naturally produce a combined, synergistic effect."

"**DXM and cannabis is a frequent combination**, which most people seem to enjoy, at least at lower doses of DXM. High doses of DXM (third plateau and up) mixed with cannabis can be very, very dissociative and sometimes unpleasant. A few people have reported that cannabis with DXM makes them feel very stupid."

	"I've received a limited number (about 20) of reports of mixing **DXM with 5HT hallucinogens, primarily LSD and mushrooms**. While one person said this combination was "not recommended", most have had incredibly profound experiences. On the other hand, very few of these have said they would ever repeat the combination, as it was simply far too powerful and terrifying. One person told me that DXM helped him avoid unpleasant cognitive effects and "bad trips" he might otherwise get from LSD alone. Regular use of DXM may alter the effects of LSD due to overall increase in 5HT binding (252) and decreased 5HT2 receptor binding (212)." "have very limited data on mixing these drugs with **DXM**. One person mixed DXM and **2CB** ("bees") and had a wonderful experience"
(e) clonazepam	10. WHITE, "Mixing DXM and Other Drugs" 2015; retrieved from Web Archive, Erowid. https://web.archive.org/web/20150422070624/https://www.erowid.org/chemicals/dxm/faq/dxm_mixing.shtml, retrieved April 22, 2015 "Some people have reported that combining **DXM** with a low dose of a **benzodiazepine** can prevent some of the more annoying side effects (mostly related to overstimulation, high blood pressure, and tachycardia). **Clonazepam** (Clonopin[tm]) in particular has been reported to have specific effects in combination with DXM, different from other benzodiazepines. These effects include enhanced CEV's (closed-eye visuals) and, of course, limiting or preventing sympathomimetic effects (high blood pressure and heart rate, sweating, etc.)."
(f) amphetamine	10. WHITE, "Mixing DXM and Other Drugs" 2015; retrieved from Web Archive, Erowid. https://web.archive.org/web/20150422070624/https://www.erowid.org/chemicals/dxm/faq/dxm_mixing.shtml, retrieved April 22, 2015 "Most who've tried it reported that **DXM** will potentiate other stimulants. Since DXM inhibits dopamine reuptake, combining it with a dopamine releasing agent (**amphetamine** or methamphetamine) will naturally produce a combined, synergistic effect."
(g) lysergamide	11. U.S. Pat. No. 8,859,579 From **claim 1**: "A method for treating a disorder associated with cephalic pain wherein said disorder is trigeminal autonomic cephalagia, comprising enterally, sublingually or parenterally administering to a subject in need of such treatment a therapeutically effective amount of a substantially pure form of **lysergic acid amide (LSA**) or bromo-lysergic acid diethylamide (bromo-LSD) present in a composition in an amount of between about 50 μg and about 5000 μg." From **claim 4**: "The method of claim 1, **further comprising administering to the subject a second compound** which acutely relieves at least one symptom of the disorder associated with cephalic pain."

	From **claim 5**: "The method of claim 4, wherein **the second compound is selected from the group consisting of oxygen, a serotonin receptor agonist, an ergot derivative,** a hormone, and a local anesthetic." From **[0012]**: "The methods of the invention can further include administering to the subject a second compound which acutely relieves at least one symptom of a disorder associated with cephalic pain, e.g., administering a compound described herein in combination with a second compound. **Examples of second compounds which acutely relieve at least one symptom of a disorder associated with cephalic pain include oxygen, serotonin receptor agonists** (e.g., triptans such as sumatriptan, eletriptan, rizatriptan, frovatriptan, almotriptan, zolmitriptan, and naratriptan), ergot derivatives (e.g., dihydroergotamine, and ergotamine tartrate)," 12. SHROOMERY, "Re: LSA and Shrooms [Re: MycoKris]" 2006; retrieved from https://www.shroomery.org/forums/showflat.php/Number/6033473#6033473, retrieved September 5, 2006 From **post# 6033473**: "My favorite psychedelic to use with **mushrooms is mescaline or lsa**. Thats not because I cant find lsd, ayahuasca or any rc's either. Lsa Adds some personality, geometry an control to the mushrooms wild visuals, adds a sort of framework. They both seem to potentiate the other, not like an maoi ofcoarse, but its as if one doesnt overpower the other. They both give what the other lacks, and what they have in common is stronger. A cool experiment is to see how little you really have to take of each. You could eat 3 grams of MG's and .5 grams of mushrooms after about an hour. Most people would be VERY suprized at how serious this mix is even at such and extreemely low dose."
6. The composition of claim 5, wherein the first serotonergic drug is lysergic acid diethylamide and the second serotonergic drug is 3,4-methylenedioxymethamphetamine.	5. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469. From p. **465**

Table IV. *Combined functional substance use reported by the sample over the past year*

	Cannabis (n = 153)	Amphetamines (n = 60)	Ecstasy (n = 43)	LSD (n = 17)	Cocaine (n = 44)	Alcohol (n = 128)
Used with [substance] to improve its effects						
cannabis	–	16	18	8	14	93
amphetamines	37	–	20	7	3	29
ecstasy	55	39	–	11	19	45
LSD	24	10	9	–	3	6
cocaine	42	4	5	1	–	45
alcohol	110	38	23	4	29	–
hallucinogenic mushrooms	2	0	0	1	0	1
	Cannabis (n = 223)	Amphetamines (n = 19)	Ecstasy (n = 15)	LSD (n = 3)	Cocaine (n = 23)	Alcohol (n = 112)
Used to help ease after effects of [substance]						
cannabis	–	5	2	0	4	18
amphetamines	83	–	6	1	1	47
ecstasy	114	7	–	3	10	59
LSD	29	0	5	–	0	13
cocaine	80	1	1	0	–	34
alcohol	70	18	7	0	14	–

7. LICHT (2012) “Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases” Hum. Psychopharmacol. Clin. Exp. 27: 352–363.

From **p. 356**

Table 2. Lifetime history of simultaneous substance use

	MDMA (%)			Psilocybin (%)			LSD (%)		
Combined with	Rarely	Often	Always	Rarely	Often	Always	Rarely	Often	Always
Alcohol	16	28	52	10	33	21	12	33	34
Cannabis	20	32	30	17	34	30	16	28	34
Amphetamines	31	26	12	15	6	7	18	6	7
MDMA	—	—	—	21	9	1	31	15	6
Cocaine	34	12	1	14	5	0	13	4	1
Psilocybin	18	10	0	—	—	—	18	6	1
Inhalants	11	5	0	9	1	1	16	3	0
LSD	32	9	1	15	6	0	—	—	—
Opioids	3	5	2	1	1	0	7	3	0
Benzodiazepines	9	6	0	3	5	0	7	0	0
Phenethylamines[a]	24	1	1	10	1	0	21	1	0
Ketamine	18	3	0	7	1	1	13	3	0
GHB	18	5	0	8	2	0	13	4	0

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
[a]Phenethylamines: 2C-B, 2C-E, 2C-I, 2C-T-4, 2C-T-7. Values shown are percentages of MDMA (n = 93), psilocybin (n = 86), or LSD (n = 67) users combining at different frequencies with each of the compounds listed on the left. Frequency categories: “rarely” (<10%), “often” (~50%), and “always” (>90%). Each user may be counted in more than one substance category.

From **p. 356**

Table 3. Substance co-administration at last recalled administration of each substance

	Any	Alcohol	Cannabis	Amphetamines	MDMA	Cocaine	Other
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Amphetamines (93)	90 (82–95)	84 (75–91)	35 (27–46)	—	13 (7–21)	10 (5–18)	25 (17–34)
MDMA (93)	92 (85–97)	77 (68–85)	49 (40–59)	23 (15–32)	—	17 (11–26)	39 (29–49)
Cocaine (91)	97 (90–99)	87 (78–92)	40 (30–50)	13 (8–22)	14 (8–23)	—	21 (14–30)
Psilocybin (86)	69 (58–77)	44 (34–55)	44 (34–55)	10 (5–19)	9 (5–18)	2 (0–9)	24 (17–35)
Inhalants (77)	75 (65–84)	53 (42–64)	23 (15–34)	6 (2–15)	13 (7–22)	4 (1–11)	30 (21–41)
LSD (67)	90 (80–95)	63 (51–73)	46 (35–58)	10 (5–20)	16 (9–27)	6 (2–15)	40 (29–52)
Opioids (60)	60 (47–71)	38 (27–51)	33 (23–46)	5 (1–14)	7 (2–16)	3 (0–12)	8 (3–18)
Benzodiazepines (57)	81 (68–89)	47 (35–60)	35 (24–48)	23 (14–35)	14 (7–26)	9 (3–19)	18 (10–30)
GHB (49)	65 (51–77)	35 (23–49)	33 (21–47)	12 (5–25)	6 (1–17)	8 (3–20)	14 (7–27)
Ketamine (49)	82 (68–90)	59 (45–72)	43 (30–57)	12 (5–25)	12 (5–25)	10 (4–22)	39 (26–53)

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
Percentages of users of each substance in the left column reporting co-administration with any substance (excluding tobacco), alcohol, cannabis, amphetamines, MDMA, cocaine, or other substances at the last recalled use. 95% confidence intervals are given in parentheses. The number of user reports for each substance is given in parentheses in the left column. Each substance user may be counted in more than one substance category.

9. SCHECHTER (1998) “‘Candyflipping’: Synergistic discriminative effect of LSD and MDMA” European Journal of Pharmacology. 314: 131-134.

	From **pg.131**: "The co-administration of d-lysergic acid diethylamide (**LSD; `Acid'**) and 3,4-methylenedioxymethamphetamine (**MDMA; `Ecstasy';** `XTC'), has reached a prevalence that has allowed for the street terminology `candyflipping' to describe the combination. Internet sites indicate a significant enhancement of central effects with their simultaneous use." From **pg.131**: "Co-administration of these doses of **MDMA and LSD** synergized to produce a maximal MDMA-like response. The possible mechanism for synergistic action upon central serotonergic neurons is discussed to explain the observed effect."
7. The composition of claim 2, wherein the second serotonergic drug is chosen from;	
(a) N,N-Dimethyl-5-hydroxy-T	1. CHILTON (1979) "Psilocin, Bufotenine and Serotonin: Historical and Biosynthetic Observations" Journal of Psychedelic Drugs. 11(1-2). From **p. 66** "If such a tryptophan-epoxide could be prepared in the laboratory, it would be expected to have only a very short lifetime, opening spontaneously to either 4-hydroxytryptophan, a potential precursor to the 4-hydroxytryptamine series (psilocin, psilocybin, baeocystin) or to the **5-hydroxy series, serotonin and bufotenine...The question is particularly pertinent for those species and genera which produce both 4-hydroxy- and 5-hydroxytryptamines together**" 2. FOZARD (1978) "Dual mechanism of the stimulant action of N,N-dimethyl-5-hydroxytryptamine (bufotenine) on cardiac sympathetic nerves" European Journal of Pharmacology. 49(1):25-30. From **p. 25** "**N,N-Dimethyl-5-hydroxytryptamine (bufotenine)** is a potent stimulant of tryptamine receptors on a variety of smooth muscle (Vane, 1959; Barlow and Khan, 1959; Bertaccini and Zamboni, 1961) and nervous (Gyermek and Bindler, 1962; Haefely, 1974a) preparations." 4. OTT (1999) "Human Pharmacology of Oral DMT Plus Harmine" Journal of Psychoactive Drugs. 31(2):171-177. From **p.171** "However, a paricá snuff of the Piaroa Indians of the Venezuelan Orinoco region contained tryptamines--**5-OH-DMT [bufotenine]**, DMT and 5MeO-DMT -together with the ß-carboline alkaloid harmine."
(b) alpha-Methyl-T;	1. CHILTON (1979) "Psilocin, Bufotenine and Serotonin: Historical and Biosynthetic Observations" Journal of Psychedelic Drugs. 11(1-2). From **p. 66** "Using the miniculture technique we found that a wide range of tryptamines, including the unnatural substrates diethyltryptamine (DET) and **alpha-methyl-tryptamine (AMT),** were readily absorbed by the mycelia and translocated into developing mushrooms.

	8. TITTARELLI (2015) “Recreational Use, Analysis and Toxicity of Tryptamines” Current Neuropharmacology. 13: 26-46. From **p.28** "**Alpha-methyltryptamine (AMT)** was firstly developed as an **antidepressant agent** called as INDOPAN, in 1960’s by the Upjohn Company and used for a short period of time in the former Soviet Union [20], but at last it was recognized as a toxic substance able to produce psychosis [21]. AMT activity is linked with the release of dopamine and its re-uptake inhibition. **AMT also acts on serotonin** and noradrenaline receptors and inhibits MAO activity in vitro and in vivo, therefore it is active after oral administration."
(c) N,N-Diethyl-T;	1. CHILTON (1979) “Psilocin, Bufotenine and Serotonin: Historical and Biosynthetic Observations” Journal of Psychedelic Drugs. 11(1-2). From **p. 66** "Using the miniculture technique we found that a wide range of tryptamines, including the unnatural substrates **diethyltryptamine (DET)** and alpha-methyl-tryptamine (AMT**),** were readily absorbed by the mycelia and translocated into developing mushrooms.”
(d) N,N-Dimethyl-T;	1. CHILTON (1979) “Psilocin, Bufotenine and Serotonin: Historical and Biosynthetic Observations” Journal of Psychedelic Drugs. 11(1-2). From **p. 66** “We noted that deuterated tryptamine was incorporated more efficiently into psilocin and psilocybin than were monomethyltryptamine (MMT) or **dimethyltryptamine (DMT)**. Both of the latter two were incorporated, however, without prior demethylation to tryptamine." 3. SHULGIN (1997) Tihkal: Tryptamines I Have Known And Loved: The Chemistry Continues. Transform Press ISBN:0-9630096-9-9. From **48_tryptamines line. 256** “**DMT and 5-MeO-DMT are the mainstay chemicals in most snuffs, and can be introduced into the product from any of several plants**” From **48_tryptamines line. 261** “With several of the experimental subjects in this study, the **DMT was preceded by the administration of 1-methyl-d-lysergic acid butanolamide (UML-491), a potent serotonin antagonist**.” 4. OTT (1999) “Human Pharmacology of Oral DMT Plus Harmine” Journal of Psychoactive Drugs. 31(2):171-177. From **p. 171** “A summary is presented of human self-experiments or psychonautic bioassays of pharmahuasca - capsules containing crystalline **N,N-dimethyltryptamine (DMT) plus harmine, as well as combinations of other psychoactive tryptamines with other ß-carbolines.**” From **p.171** "A 1967 analysis of a half-dozen South American snuffs used in shamanic healing by the Tucano, Waiká , Araraibo, Piaroa and Surára Indians, showed all but one of the powders to contain tryptamines, mainly **5-**

	methoxy-N,N-dimethyltryptamine [5-MeO-DMT] and secondarily N,N-dimethyltryptamine [DMT] (HOLMSTEDT & LINDGREN 1967). However, a paricá snuff of the Piaroa Indians of the Venezuelan Orinoco region contained tryptamines--5-OH-DMT [bufotenine], **DMT** and 5MeO-DMT -together with the ß-carboline alkaloid harmine." 8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46. From p. 29 "**DMT binds several serotonin receptors, acting as a partial agonist in particular on the 5-HT2A and 5-HT2C receptors.**" From **p. 40** ""An unidentified peak was detected in both the blood and urine specimen on the alkaline drug screen: subsequent mass spectral analysis identified the substance as **5-MeO-DMT**". In the heart blood sample was identified **N,N-dimethyltryptamine** (0.02 mg/L), 5-methoxy N,Ndimethyltryptamine (1.88 mg/L), tetrahydroharmine (0.38 mg/L), harmaline (0.07 mg/L), and harmine (0.17 mg/L)."
(e) 5-Methyoxy-alpha-methyl-T	8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46. From **p. 28** "Furthermore, he discovered that **5-MeO-AMT**, "inhibited monoamine (dopamine, 5-HT and norepinephrine) re-uptake and stimulated monoamine release; its potency was second to that of AMT."
(f) alpha-Ethyl-T	8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46. From **p.29** "Also **alpha-ethyltryptamine (AET)** was firstly introduced as **an antidepressant agent** by Upjohn company in 1960s with the name MONASE, but it was withdrawn from the market because of an unacceptable incidence of idiosyncratic agranulocytosis. AET may induce serotonin neurotoxicity [26]"
(g) N-Dimethyl-T	8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines". Current Neuropharmacology 13: 26-46. From p. 29 "Further, tryptamine undergoes a methylation process, generating the intermediate product **N-methyltryptamine (NMT). NMT is in turn transmethylated to form the final product N,N-dimethyl tryptamine.**"
(h) N,N-Diethyl-T	8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46. From **p.29** "Its mechanism of action is not clear, but, like other psychedelic tryptamines, **DET** could present an agonist activity towards serotonin receptors [31, 32]."

(i) N,N-Dipropyl-T	8. TITTARELLI (2015) “Recreational Use, Analysis and Toxicity of Tryptamines” Current Neuropharmacology. 13: 26-46. From **p.29** "There are few peer-reviewed experimental studies that try to explain the ways of interaction among **DPT** and serotonin receptors: Nagai revealed a strong inhibition of 5-HT reuptake in rat synaptosomes [16], and Thiagaraj also observed a moderate affinity partial agonism at the human 5-HT1A receptor [34]."
(j) N,N-Diisopropyl-T	8. TITTARELLI (2015) “Recreational Use, Analysis and Toxicity of Tryptamines” Current Neuropharmacology. 13: 26-46. From **p.29** "**Diisopropyl-tryptamine (DiPT)**...It is an agonist at 5HT2A receptors and a partial agonist at 5HT1A receptors [37], but 5-HT1A activity “is not thought to be necessary for hallucinogenic effects” [38]. Furthermore, DiPT blocks the serotonin uptake and it has little interaction with dopamine or norepinephrine transporters [16]."
(k) 5-Methoxy-N,N-dimethyl-T	8. TITTARELLI (2015) “Recreational Use, Analysis and Toxicity of Tryptamines” Current Neuropharmacology. 13: 26-46. From **p.31** “P.31 "**5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT)**...it has high affinity for the 5-HT1A serotonin receptor"” From **p.38** "He purchased on the Internet some Syrian rue seeds containing harmaline, a natural MAOI [76]. After ingestion of seeds, smoking 10 mg of **5-MeO-DMT**, and insufflation of further 15-20 mg, his friends found him collapsed, agitated and hallucinating. He arrived in E.D. with tachycardia (heart rate 186 bpm) and hyperpyrexia (40.7°C). He required physical restraint and clinicians administered to him 2.5 mg of IV **lorazepam**." From **p. 40** "“An unidentified peak was detected in both the blood and urine specimen on the alkaline drug screen: subsequent mass spectral analysis identified the substance as **5-MeO-DMT**”. In the heart blood sample was identified N,N-dimethyltryptamine (0.02 mg/L), **5-methoxy N,Ndimethyltryptamine** (1.88 mg/L), tetrahydroharmine (0.38 mg/L), harmaline (0.07 mg/L), and harmine (0.17 mg/L)."
8. The composition of claim 2, wherein the second serotonergic drug is chosen from;	
(a) a cannabinoid	5. BOYS (2001) “Understanding reasons for drug use amongst young people a functional perspective” Health Education Research. 16(4):457-469. From p. **465**

Table IV. *Combined functional substance use reported by the sample over the past year*

	Cannabis (n = 153)	Amphetamines (n = 60)	Ecstasy (n = 43)	LSD (n = 17)	Cocaine (n = 44)	Alcohol (n = 128)
Used with [substance] to improve its effects						
cannabis	–	16	18	8	14	93
amphetamines	37	–	20	7	3	29
ecstasy	55	39	–	11	19	45
LSD	24	10	9	–	3	6
cocaine	42	4	5	1	–	45
alcohol	110	38	23	4	29	–
hallucinogenic mushrooms	2	0	0	1	0	1
	Cannabis (n = 223)	Amphetamines (n = 19)	Ecstasy (n = 15)	LSD (n = 3)	Cocaine (n = 23)	Alcohol (n = 112)
Used to help ease after effects of [substance]						
cannabis	–	5	2	0	4	18
amphetamines	83	–	6	1	1	47
ecstasy	114	7	–	3	10	59
LSD	29	0	5	–	0	13
cocaine	80	1	1	0	–	34
alcohol	70	18	7	0	14	–

7. LICHT (2012) “Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases” Hum. Psychopharmacol. Clin. Exp. 27: 352–363.

From **p.359** "Focusing on functional causes, in the present study, seven participants stated that **cannabis** enhanced (intensified or augmented) the effects of MDMA, which is in line with a previous study where 36% of cannabis users used cannabis to “improve the effects” of ecstasy (Boys et al., 2001)."

From **p. 356**

Table 2. Lifetime history of simultaneous substance use

	MDMA (%)			Psilocybin (%)			LSD (%)		
Combined with	Rarely	Often	Always	Rarely	Often	Always	Rarely	Often	Always
Alcohol	16	28	52	10	33	21	12	33	34
Cannabis	20	32	30	17	34	30	16	28	34
Amphetamines	31	26	12	15	6	7	18	6	7
MDMA	—	—	—	21	9	1	31	15	6
Cocaine	34	12	1	14	5	0	13	4	1
Psilocybin	18	10	0	—	—	—	18	6	1
Inhalants	11	5	0	9	1	1	16	3	0
LSD	32	9	1	15	6	0	—	—	—
Opioids	3	5	2	1	1	0	7	3	0
Benzodiazepines	9	6	0	3	5	0	7	0	0
Phenethylamines[a]	24	1	1	10	1	0	21	1	0
Ketamine	18	3	0	7	1	1	13	3	0
GHB	18	5	0	8	2	0	13	4	0

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
[a]Phenethylamines: 2C-B, 2C-E, 2C-I, 2C-T-4, 2C-T-7. Values shown are percentages of MDMA (n = 93), psilocybin (n = 86), or LSD (n = 67) users combining at different frequencies with each of the compounds listed on the left. Frequency categories: “rarely” (<10%), “often” (~50%), and “always” (>90%). Each user may be counted in more than one substance category.

From **p. 356**

Table 3. Substance co-administration at last recalled administration of each substance

	Any	Alcohol	Cannabis	Amphetamines	MDMA	Cocaine	Other
Cannabis (98)	62 (52–71)	52 (42–62)	—	5 (2–12)	7 (3–14)	3 (1–9)	22 (15–32)
Amphetamines (93)	90 (82–95)	84 (75–91)	35 (27–46)	—	13 (7–21)	10 (5–18)	25 (17–34)
MDMA (93)	92 (85–97)	77 (68–85)	49 (40–59)	23 (15–32)	—	17 (11–26)	39 (29–49)
Cocaine (91)	97 (90–99)	87 (78–92)	40 (30–50)	13 (8–22)	14 (8–23)	—	21 (14–30)
Psilocybin (86)	69 (58–77)	44 (34–55)	44 (34–55)	10 (5–19)	9 (5–18)	2 (0–9)	24 (17–35)
Inhalants (77)	75 (65–84)	53 (42–64)	23 (15–34)	6 (2–15)	13 (7–22)	4 (1–11)	30 (21–41)
LSD (67)	90 (80–95)	63 (51–73)	46 (35–58)	10 (5–20)	16 (9–27)	6 (2–15)	40 (29–52)
Opioids (60)	60 (47–71)	38 (27–51)	33 (23–46)	5 (1–14)	7 (2–16)	3 (0–12)	8 (3–18)
Benzodiazepines (57)	81 (68–89)	47 (35–60)	35 (24–48)	23 (14–35)	14 (7–26)	9 (3–19)	18 (10–30)
GHB (49)	65 (51–77)	35 (23–49)	33 (21–47)	12 (5–25)	6 (1–17)	8 (3–20)	14 (7–27)
Ketamine (49)	82 (68–90)	59 (45–72)	43 (30–57)	12 (5–25)	12 (5–25)	10 (4–22)	39 (26–53)

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
Percentages of users of each substance in the left column reporting co-administration with any substance (excluding tobacco), alcohol, cannabis, amphetamines, MDMA, cocaine, or other substances at the last recalled use. 95% confidence intervals are given in parentheses. The number of user reports for each substance is given in parentheses in the left column. Each substance user may be counted in more than one substance category.

(b) lysergic acid diethylamide

5. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469.

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Cocaine	34	12	1	14	5	0	13	4	1
Psilocybin	18	10	0	—	—	—	18	6	1
Inhalants	11	5	0	9	1	1	16	3	0
LSD	32	9	1	15	6	0	—	—	—
Opioids	3	5	2	1	1	0	7	3	0
Benzodiazepines	9	6	0	3	5	0	7	0	0
Phenethylamines[a]	24	1	1	10	1	0	21	1	0
Ketamine	18	3	0	7	1	1	13	3	0
GHB	18	5	0	8	2	0	13	4	0

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
[a]Phenethylamines: 2C-B, 2C-E, 2C-I, 2C-T-4, 2C-T-7. Values shown are percentages of MDMA (n = 93), psilocybin (n = 86), or LSD (n = 67) users combining at different frequencies with each of the compounds listed on the left. Frequency categories: "rarely" (<10%), "often" (~50%), and "always" (>90%). Each user may be counted in more than one substance category.

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MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
Percentages of users of each substance in the left column reporting co-administration with any substance (excluding tobacco), alcohol, cannabis, amphetamines, MDMA, cocaine, or other substances at the last recalled use. 95% confidence intervals are given in parentheses. The number of user reports for each substance is given in parentheses in the left column. Each substance user may be counted in more than one substance category.

(c) 3,4-methylenedioxymethamphetamine

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(d) dextromethorphan

10. WHITE, "Mixing DXM and Other Drugs" 2015; retrieved from Web Archive, Erowid. https://web.archive.org/web/20150422070624/https://www.erowid.org/chemicals/dxm/faq/dxm_mixing.shtml, retrieved April 22, 2015

"Some people have reported that combining **DXM** with a low dose of a **benzodiazepine** can prevent some of the more annoying side effects (mostly related to overstimulation, high blood pressure, and tachycardia). **Clonazepam** (Clonopin[tm]) in particular has been reported to have specific effects in combination with DXM, different from other benzodiazepines. These effects include enhanced CEV's (closed-eye visuals) and, of course, limiting or preventing sympathomimetic effects (high blood pressure and heart rate, sweating, etc.)."

"Most who've tried it reported that **DXM** will potentiate other stimulants. Since DXM inhibits dopamine reuptake, combining it with a dopamine releasing agent (**amphetamine** or methamphetamine) will naturally produce a combined, synergistic effect."

"**DXM and cannabis is a frequent combination**, which most people seem to enjoy, at least at lower doses of DXM. High doses of DXM (third plateau and up) mixed with cannabis can be very, very dissociative and sometimes unpleasant. A few people have reported that cannabis with DXM makes them feel very stupid."

	"I've received a limited number (about 20) of reports of mixing **DXM with 5HT hallucinogens, primarily LSD and mushrooms**. While one person said this combination was "not recommended", most have had incredibly profound experiences. On the other hand, very few of these have said they would ever repeat the combination, as it was simply far too powerful and terrifying. One person told me that DXM helped him avoid unpleasant cognitive effects and "bad trips" he might otherwise get from LSD alone. Regular use of DXM may alter the effects of LSD due to overall increase in 5HT binding (252) and decreased 5HT2 receptor binding (212)." "have very limited data on mixing these drugs with **DXM**. One person mixed DXM and **2CB** ("bees") and had a wonderful experience"
(e) clonazepam	10. WHITE, "Mixing DXM and Other Drugs" 2015; retrieved from Web Archive, Erowid. https://web.archive.org/web/20150422070624/https://www.erowid.org/chemicals/dxm/faq/dxm_mixing.shtml, retrieved April 22, 2015 "Some people have reported that combining **DXM** with a low dose of a **benzodiazepine** can prevent some of the more annoying side effects (mostly related to overstimulation, high blood pressure, and tachycardia). **Clonazepam** (Clonopin[tm]) in particular has been reported to have specific effects in combination with DXM, different from other benzodiazepines. These effects include enhanced CEV's (closed-eye visuals) and, of course, limiting or preventing sympathomimetic effects (high blood pressure and heart rate, sweating, etc.)."
(f) amphetamine	10. WHITE, "Mixing DXM and Other Drugs" 2015; retrieved from Web Archive, Erowid. https://web.archive.org/web/20150422070624/https://www.erowid.org/chemicals/dxm/faq/dxm_mixing.shtml, retrieved April 22, 2015 "Most who've tried it reported that **DXM** will potentiate other stimulants. Since DXM inhibits dopamine reuptake, combining it with a dopamine releasing agent (**amphetamine** or methamphetamine) will naturally produce a combined, synergistic effect."
(g) lorazepam	8. TITTARELLI (2015) "Recreational Use, Analysis and Toxicity of Tryptamines" Current Neuropharmacology. 13: 26-46. From **p.38** "He purchased on the Internet some Syrian rue seeds containing harmaline, a natural MAOI [76]. After ingestion of seeds, smoking 10 mg of **5-MeO-DMT**, and insufflation of further 15-20 mg, his friends found him collapsed, agitated and hallucinating. He arrived in E.D. with tachycardia (heart rate 186 bpm) and hyperpyrexia (40.7°C). He required physical restraint and clinicians administered to him 2.5 mg of IV **lorazepam**."
(h) lysergamide	11. U.S. Pat. No. 8,859,579

	From **claim 1**: "A method for treating a disorder associated with cephalic pain wherein said disorder is trigeminal autonomic cephalagia, comprising enterally, sublingually or parenterally administering to a subject in need of such treatment a therapeutically effective amount of a substantially pure form of **lysergic acid amide (LSA)** or bromo-lysergic acid diethylamide (bromo-LSD) present in a composition in an amount of between about 50 μg and about 5000 μg." From **claim 4**: "The method of claim 1, **further comprising administering to the subject a second compound** which acutely relieves at least one symptom of the disorder associated with cephalic pain." From **claim 5**: "The method of claim 4, wherein **the second compound is selected from the group consisting of oxygen, a serotonin receptor agonist, an ergot derivative,** a hormone, and a local anesthetic." From **[0012]**: "The methods of the invention can further include administering to the subject a second compound which acutely relieves at least one symptom of a disorder associated with cephalic pain, e.g., administering a compound described herein in combination with a second compound. **Examples of second compounds which acutely relieve at least one symptom of a disorder associated with cephalic pain include oxygen, serotonin receptor agonists** (e.g., triptans such as sumatriptan, eletriptan, rizatriptan, frovatriptan, almotriptan, zolmitriptan, and naratriptan), ergot derivatives (e.g., dihydroergotamine, and ergotamine tartrate)," 12. SHROOMERY, "Re: LSA and Shrooms [Re: MycoKris]" 2006; retrieved from https://www.shroomery.org/forums/showflat.php/Number/6033473#6033473, retrieved September 5, 2006 From **post# 6033473**: "My favorite psychedelic to use with **mushrooms is mescaline or lsa**. Thats not because I cant find lsd, ayahuasca or any rc's either. Lsa Adds some personality, geometry an control to the mushrooms wild visuals, adds a sort of framework. They both seem to potentiate the other, not like an maoi ofcoarse, but its as if one doesnt overpower the other. They both give what the other lacks, and what they have in common is stronger. A cool experiment is to see how little you really have to take of each. You could eat 3 grams of MG's and .5 grams of mushrooms after about an hour. Most people would be VERY suprized at how serious this mix is even at such and extreemely low dose."
9. The composition of claim 8, wherein the second serotonergic drug is chosen from 3,4-methylenedioxymetham	5. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469. From p. **465**

phetamine and lysergic acid diethylamide.

Table IV. *Combined functional substance use reported by the sample over the past year*

	Cannabis (n = 153)	Amphetamines (n = 60)	Ecstasy (n = 43)	LSD (n = 17)	Cocaine (n = 44)	Alcohol (n = 128)
Used with [substance] to improve its effects						
cannabis	–	16	18	8	14	93
amphetamines	37	–	20	7	3	29
ecstasy	55	39	–	11	19	45
LSD	24	10	9	–	3	6
cocaine	42	4	5	1	–	45
alcohol	110	38	23	4	29	–
hallucinogenic mushrooms	2	0	0	1	0	1
	Cannabis (n = 223)	Amphetamines (n = 19)	Ecstasy (n = 15)	LSD (n = 3)	Cocaine (n = 23)	Alcohol (n = 112)
Used to help ease after effects of [substance]						
cannabis	–	5	2	0	4	18
amphetamines	83	–	6	1	1	47
ecstasy	114	7	–	3	10	59
LSD	29	0	5	–	0	13
cocaine	80	1	1	0	–	34
alcohol	70	18	7	0	14	–

7. LICHT (2012) “Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases” Hum. Psychopharmacol. Clin. Exp. 27: 352–363.

From **p. 352** “SPU was prevalent among **MDMA, D-lysergic acid diethylamide (LSD),** and psilocybin users, in particular with alcohol and cannabis.
Among MDMA users, 69% had combined MDMA with amphetamines, 56% with hallucinogens, and 47% with cocaine.”

From **p.360** "Such enhancing effects were also reported by polydrug users in the UK, where **65% of LSD users had taken LSD to “improve the effects” of MDMA and 21% of MDMA users had taken MDMA to “improve the effects” of LSD** (Boys et al., 2001)."

From **p. 356**

Table 2. Lifetime history of simultaneous substance use

	MDMA (%)			Psilocybin (%)			LSD (%)		
Combined with	Rarely	Often	Always	Rarely	Often	Always	Rarely	Often	Always
Alcohol	16	28	52	10	33	21	12	33	34
Cannabis	20	32	30	17	34	30	16	28	34
Amphetamines	31	26	12	15	6	7	18	6	7
MDMA	—	—	—	21	9	1	31	15	6
Cocaine	34	12	1	14	5	0	13	4	1
Psilocybin	18	10	0	—	—	—	18	6	1
Inhalants	11	5	0	9	1	1	16	3	0
LSD	32	9	1	15	6	0	—	—	—
Opioids	3	5	2	1	1	0	7	3	0
Benzodiazepines	9	6	0	3	5	0	7	0	0
Phenethylamines[a]	24	1	1	10	1	0	21	1	0
Ketamine	18	3	0	7	1	1	13	3	0
GHB	18	5	0	8	2	0	13	4	0

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
[a]Phenethylamines: 2C-B, 2C-E, 2C-I, 2C-T-4, 2C-T-7. Values shown are percentages of MDMA (n = 93), psilocybin (n = 86), or LSD (n = 67) users combining at different frequencies with each of the compounds listed on the left. Frequency categories: “rarely” (<10%), “often” (~50%), and “always” (>90%). Each user may be counted in more than one substance category.

From **p. 356**

	Table 3. Substance co-administration at last recalled administration of each substance | | Any | Alcohol | Cannabis | Amphetamines | MDMA | Cocaine | Other | |---|---|---|---|---|---|---|---| | Cannabis (98) | 62 (52–71) | 52 (42–62) | — | 5 (2–12) | 7 (3–14) | 3 (1–9) | 22 (15–32) | | Amphetamines (93) | 90 (82–95) | 84 (75–91) | 35 (27–46) | — | 13 (7–21) | 10 (5–18) | 25 (17–34) | | MDMA (93) | 92 (85–97) | 77 (68–85) | 49 (40–59) | 23 (15–32) | — | 17 (11–26) | 39 (29–49) | | Cocaine (91) | 97 (90–99) | 87 (78–92) | 40 (30–50) | 13 (8–22) | 14 (8–23) | — | 21 (14–30) | | Psilocybin (86) | 69 (58–77) | 44 (34–55) | 44 (34–55) | 10 (5–19) | 9 (5–18) | 2 (0–9) | 24 (17–35) | | Inhalants (77) | 75 (65–84) | 53 (42–64) | 23 (15–34) | 6 (2–15) | 13 (7–22) | 4 (1–11) | 30 (21–41) | | LSD (67) | 90 (80–95) | 63 (51–73) | 46 (35–58) | 10 (5–20) | 16 (9–27) | 6 (2–15) | 40 (29–52) | | Opioids (60) | 60 (47–71) | 38 (27–51) | 33 (23–46) | 5 (1–14) | 7 (2–16) | 3 (0–12) | 8 (3–18) | | Benzodiazepines (57) | 81 (68–89) | 47 (35–60) | 35 (24–48) | 23 (14–35) | 14 (7–26) | 9 (3–19) | 18 (10–30) | | GHB (49) | 65 (51–77) | 35 (23–49) | 33 (21–47) | 12 (5–25) | 6 (1–17) | 8 (3–20) | 14 (7–27) | | Ketamine (49) | 82 (68–90) | 59 (45–72) | 43 (30–57) | 12 (5–25) | 12 (5–25) | 10 (4–22) | 39 (26–53) | MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid. Percentages of users of each substance in the left column reporting co-administration with any substance (excluding tobacco), alcohol, cannabis, amphetamines, MDMA, cocaine, or other substances at the last recalled use. 95% confidence intervals are given in parentheses. The number of user reports for each substance is given in parentheses in the left column. Each substance user may be counted in more than one substance category.
10. The composition of claim 1, wherein the first serotonergic drug is an ibogaine derivative and the second serotonergic drug is chosen from a psilocybin derivative and;	13. LEEANN, "Personal Story: Iboga And Psilocybin Mushrooms Saved Me On The Brink Of Suicide" 2015; retrieved from Web Archive, Reset https://web.archive.org/web/20151203193708/https://reset.me/personal-story/personal-story-iboga-and-magic-mushrooms-saved-me-on-the-brink-of-suicide/, retrieved December 3, 2015 "Thank you iboga and psilocybin for turning me from a suicidal, depressive person to the happiest person that I know." 17. ALPER (2008) "The ibogaine medical subculture." Journal of Ethnopharmacology. 115(1): 9-24. From **p. 15**: "Use of other **"plant medicine or fungi" in combination with ibogaine**. Pretreatment medical and psychiatric history, no medical testing" 18. U.S. Pat. App. Pub. No. 2008/0293695 From **[0039]**: "the prescribing of a drug product containing **at least one drug substance** as an organic acid addition salt of an amine containing API to a patient by a defined method of administration wherein the drug substance is a prophylactic in a different method of administration." From **claim** 1: "1. A drug substance comprising a pharmaceutically acceptable organic acid addition salt of an amine containing pharmaceutically active compound useful for the treatment of an ailment by therapeutic administration and exhibiting anti-abuse properties when employed in non-therapeutic administration." From **claim 7**: "The drug substance of claim 1 wherein said pharmaceutically active compound comprises a material selected from acetaminophen, caffeine, acetorphine, acetylmethadol, allylprodine, alphacetylmethadol, **bufotenine**, dextromoramide, diethyltryptamine, etorphine, heroin, **ibogaine**, ketobemidone, lysergic acid diethylamide, mescaline, methaqualone, 3,4-methylenedioxyamphetamine, 3,4-methylenedioxymethamphetamine, N-ethyl-1-phenylcyclohexylamine, peyote, 1-(1-phenylcyclohexyl)pyrrolidine, **psilocybin, psilocin**, 1-{1-(2-thienyl)-cyclohexyl}-piperidine, alphaprodine, anileridine, cocaine, dextropropoxyphene, diphenoxylate, ethylmorphine, glutethimide, hydrocodone, hydromorphone, levo-alphaacetylmethadol, levorphanol, meperidine, methadone, morphine, opium, oxycodone, oxymorphone, poppy

	straw, thebaine, amphetamine, methamphetamine, methylphenidate, phencyclidine, codeine, benzphetamine, ketamine, alprazolam, chlorodiazepoxide, clorazepate, diethylpropion, fenfluramine, flurazepam, halazepam, lorazepam, mazindol, mebutamate, midazolam, oxazepam, pemoline, pentazocine, phentermine, prazepam, quazepam, temazepam, triazolam, zolpidem, and buprenorphine."
11. The composition of claim 10, wherein the second serotonergic drug is 3,4-methylenedioxymethamphetamine.	18. U.S. Pat. App. Pub. No. 2008/0293695 From **[0039]**: "the prescribing of a drug product containing **at least one drug substance** as an organic acid addition salt of an amine containing API to a patient by a defined method of administration wherein the drug substance is a prophylactic in a different method of administration." From **claim** 1: "1. A drug substance comprising a pharmaceutically acceptable organic acid addition salt of an amine containing pharmaceutically active compound useful for the treatment of an ailment by therapeutic administration and exhibiting anti-abuse properties when employed in non-therapeutic administration." From **claim 7**: "The drug substance of claim 1 wherein said pharmaceutically active compound comprises a material selected from acetaminophen, caffeine, acetorphine, acetylmethadol, allylprodine, alphacetylmethadol, **bufotenine**, dextromoramide, diethyltryptamine, etorphine, heroin, **ibogaine**, ketobemidone, lysergic acid diethylamide, mescaline, methaqualone, 3,4-methylenedioxyamphetamine, 3,4-methylenedioxymethamphetamine, N-ethyl-1-phenylcyclohexylamine, peyote, 1-(1-phenylcyclohexyl)pyrrolidine, **psilocybin, psilocin**, 1-{1-(2-thienyl)-cyclohexyl}-piperidine, alphaprodine, anileridine, cocaine, dextropropoxyphene, diphenoxylate, ethylmorphine, glutethimide, hydrocodone, hydromorphone, levo-alphaacetylmethadol, levorphanol, meperidine, methadone, morphine, opium, oxycodone, oxymorphone, poppy straw, thebaine, amphetamine, methamphetamine, methylphenidate, phencyclidine, codeine, benzphetamine, ketamine, alprazolam, chlorodiazepoxide, clorazepate, diethylpropion, fenfluramine, flurazepam, halazepam, lorazepam, mazindol, mebutamate, midazolam, oxazepam, pemoline, pentazocine, phentermine, prazepam, quazepam, temazepam, triazolam, zolpidem, and buprenorphine."
12. The composition of claim 6 comprising between 10 to 500 .mu.g of lysergic acid diethylamide and between 10 to 500 mg of 3,4-methylenedioxymethamphetamine.	7. LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363. From **p. 357**: "The **average MDMA dose** used at the last recalled administration event was **185 mg (95% CI: 153–216 mg)** or around three Ecstasy tablets. At the last recalled MDMA administration, the simultaneous use of MDMA and either one of the following substances: alcohol, cannabis, amphetamines, cocaine, psilocybin, LSD, or GHB, had no significant effect on MDMA dose"

	From **p. 357**: "The effect of SPU on psilocybin or **LSD dose could not be analyzed because of high variability** in substance units reported and unknown concentration of active substance per substance unit, leading to difficulties in standardizing the doses used." 16. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **pg. 3**: "The choice and dosages of substances used for the sessions - **MDMA: 80–130 mg** - **LSD: 50–200ug** - 2-CB: 15–30 mg" From **pg. 3**: "Most psycholytic sessions began with **MDMA, then LSD or 2-CB were added** mid-way. Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or psilocybin were used. Crucially, all the participants (including Friederike and Konrad) at any given session always all took the same substance at the same time; only the doses changed between individuals."
13. The composition of claim 12 comprising between 50 to 250 .mu.g of lysergic acid diethylamide and between 50 to 250 mg of 3,4-methylenedioxymethamphetamine.	7. LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363. From **p. 357**: "The **average MDMA dose** used at the last recalled administration event was **185 mg (95% CI: 153–216 mg)** or around three Ecstasy tablets. At the last recalled MDMA administration, the simultaneous use of MDMA and either one of the following substances: alcohol, cannabis, amphetamines, cocaine, psilocybin, LSD, or GHB, had no significant effect on MDMA dose" From **p. 357**: "The effect of SPU on psilocybin or **LSD dose could not be analyzed because of high variability** in substance units reported and unknown concentration of active substance per substance unit, leading to difficulties in standardizing the doses used." 16. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **pg. 3**: "The choice and dosages of substances used for the sessions - **MDMA: 80–130 mg** - **LSD: 50–200ug** - 2-CB: 15–30 mg"

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14. The composition of claim 13 comprising 100 .mu.g of lysergic acid diethylamide and 100 mg of 3,4-methylenedioxymethamphetamine.	16. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **pg. 3**: "The choice and dosages of substances used for the sessions - **MDMA: 80–130 mg** - **LSD: 50–200ug** - 2-CB: 15–30 mg" From **pg. 3**: "Most psycholytic sessions began with **MDMA, then LSD or 2-CB were added** mid-way. Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or psilocybin were used. Crucially, all the participants (including Friederike and Konrad) at any given session always all took the same substance at the same time; only the doses changed between individuals."
15. A method of treating a psychological disorder comprising administering a first serotonergic drug and a second serotonergic drug to a subject in need of treatment.	14. SZEGEDI (1996) "Combination treatment with clomipramine and fluvoxamine: drug monitoring, safety, and tolerability data" J. Clin. Psychiatry. 57(6):257-264. From **p. 257**: "We report tolerability and safety of **combined treatment with fluvoxamine and clomipramine** (CMI) in 22 patients. Most patients suffered from **depression and obsessive-compulsive symptoms**." 15. SHELTON (2005) "Olanzapine/fluoxetine combination for treatment-resistant depression: a controlled study of SSRI and nortriptyline resistance" J. Clin. Psychiatry. 66(10):1289-1297. From **p. 1289**: "This 8-week, double-blind, multicenter study was undertaken to replicate, in a larger sample of patients with **treatment-resistant major depressive disorder** (MDD; DSM-IV criteria), the results of a pilot study of the **olanzapine/fluoxetine combination**."
16. The method of claim 15, wherein the first serotonergic drug is lysergic acid diethylamide and the second serotonergic drug is 3,4-methylenedioxymethamphetamine.	5. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469. From p. **465**

Table IV. *Combined functional substance use reported by the sample over the past year*

	Cannabis (n = 153)	Amphetamines (n = 60)	Ecstasy (n = 43)	LSD (n = 17)	Cocaine (n = 44)	Alcohol (n = 128)
Used with [substance] to improve its effects						
cannabis	–	16	18	8	14	93
amphetamines	37	–	20	7	3	29
ecstasy	55	39	–	11	19	45
LSD	24	10	9	–	3	6
cocaine	42	4	5	1	–	45
alcohol	110	38	23	4	29	–
hallucinogenic mushrooms	2	0	0	1	0	1
	Cannabis (n = 223)	Amphetamines (n = 19)	Ecstasy (n = 15)	LSD (n = 3)	Cocaine (n = 23)	Alcohol (n = 112)
Used to help ease after effects of [substance]						
cannabis	–	5	2	0	4	18
amphetamines	83	–	6	1	1	47
ecstasy	114	7	–	3	10	59
LSD	29	0	5	–	0	13
cocaine	80	1	1	0	–	34
alcohol	70	18	7	0	14	–

7. LICHT (2012) “Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases” Hum. Psychopharmacol. Clin. Exp. 27: 352–363.

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Among MDMA users, 69% had combined MDMA with amphetamines, 56% with hallucinogens, and 47% with cocaine.”

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From **p. 356**

Table 2. Lifetime history of simultaneous substance use

	MDMA (%)			Psilocybin (%)			LSD (%)		
Combined with	Rarely	Often	Always	Rarely	Often	Always	Rarely	Often	Always
Alcohol	16	28	52	10	33	21	12	33	34
Cannabis	20	32	30	17	34	30	16	28	34
Amphetamines	31	26	12	15	6	7	18	6	7
MDMA	—	—	—	21	9	1	31	15	6
Cocaine	34	12	1	14	5	0	13	4	1
Psilocybin	18	10	0	—	—	—	18	6	1
Inhalants	11	5	0	9	1	1	16	3	0
LSD	32	9	1	15	6	0	—	—	—
Opioids	3	5	2	1	1	0	7	3	0
Benzodiazepines	9	6	0	3	5	0	7	0	0
Phenethylamines[a]	24	1	1	10	1	0	21	1	0
Ketamine	18	3	0	7	1	1	13	3	0
GHB	18	5	0	8	2	0	13	4	0

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
[a]Phenethylamines: 2C-B, 2C-E, 2C-I, 2C-T-4, 2C-T-7. Values shown are percentages of MDMA (n = 93), psilocybin (n = 86), or LSD (n = 67) users combining at different frequencies with each of the compounds listed on the left. Frequency categories: “rarely” (<10%), “often” (~50%), and “always” (>90%). Each user may be counted in more than one substance category.

From **p. 356**

Table 3. Substance co-administration at last recalled administration of each substance

	Any	Alcohol	Cannabis	Amphetamines	MDMA	Cocaine	Other
Cannabis (98)	62 (52–71)	52 (42–62)	—	5 (2–12)	7 (3–14)	3 (1–9)	22 (15–32)
Amphetamines (93)	90 (82–95)	84 (75–91)	35 (27–46)	—	13 (7–21)	10 (5–18)	25 (17–34)
MDMA (93)	92 (85–97)	77 (68–85)	49 (40–59)	23 (15–32)	—	17 (11–26)	39 (29–49)
Cocaine (91)	97 (90–99)	87 (78–92)	40 (30–50)	13 (8–22)	14 (8–23)	—	21 (14–30)
Psilocybin (86)	69 (58–77)	44 (34–55)	44 (34–55)	10 (5–19)	9 (5–18)	2 (0–9)	24 (17–35)
Inhalants (77)	75 (65–84)	53 (42–64)	23 (15–34)	6 (2–15)	13 (7–22)	4 (1–11)	30 (21–41)
LSD (67)	90 (80–95)	63 (51–73)	46 (35–58)	10 (5–20)	16 (9–27)	6 (2–15)	40 (29–52)
Opioids (60)	60 (47–71)	38 (27–51)	33 (23–46)	5 (1–14)	7 (2–16)	3 (0–12)	8 (3–18)
Benzodiazepines (57)	81 (68–89)	47 (35–60)	35 (24–48)	23 (14–35)	14 (7–26)	9 (3–19)	18 (10–30)
GHB (49)	65 (51–77)	35 (23–49)	33 (21–47)	12 (5–25)	6 (1–17)	8 (3–20)	14 (7–27)
Ketamine (49)	82 (68–90)	59 (45–72)	43 (30–57)	12 (5–25)	12 (5–25)	10 (4–22)	39 (26–53)

MDMA, 3,4-methylenedioxymethamphetamine; LSD, D-lysergic acid diethylamide; GHB, gamma-hydroxybutyric acid.
Percentages of users of each substance in the left column reporting co-administration with any substance (excluding tobacco), alcohol, cannabis, amphetamines, MDMA, cocaine, or other substances at the last recalled use. 95% confidence intervals are given in parentheses. The number of user reports for each substance is given in parentheses in the left column. Each substance user may be counted in more than one substance category.

16. SESSA (2015) “Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary” Drug Science, Policy and Law. 2(0):1-8.

From **pg. 3**: “Most psycholytic sessions began with **MDMA, then LSD or 2-CB were added** mid-way. Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or psilocybin were used. Crucially, all the participants (including Friederike and Konrad) at any given session always all took the same substance at the same time; only the doses changed between individuals.”

From **pg. 4**: “In common with many psychotherapists, Friederike did not routinely collect quantitative psychological measures of her clients’ progress. But of the 97 clients who underwent psycholytic psychotherapy, the qualitative outcomes were overwhelmingly positive. There were no serious adverse reactions to the substances, no psychoses, no hospitalisations and no suicides of any clients who were actively undergoing psycholytic therapy. Almost all of the clients describe improvements in their relationships and well-being at home and work.”

17. The method of claim 16 comprising administering a composition of claim 6.

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18. The method of claim 16, wherein the psychological disorder is chosen from an anxiety disorder, a compulsive disorder, addiction, and a depressive disorder.	5. BOYS (2001) “Understanding reasons for drug use amongst young people a functional perspective” Health Education Research. 16(4):457-469. From p. 457 “The most popular functions for use were using to: relax (96.7%), become intoxicated (96.4%), keep awake at night while socializing (95.9%), enhance an activity (88.5%) and **alleviate depressed mood** (86.8%).” 7. LICHT (2012) “Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases” Hum. Psychopharmacol. Clin. Exp. 27: 352–363. From **p.359** "Also, given that the CB1 cannabinoid receptor mediates some of the rewarding properties of MDMA (Mohamed et al., 2011), **cannabis consumption when the central concentration of MDMA tapers may counteract feelings of depression and anhedonia**." 8. TITTARELLI (2015) “Recreational Use, Analysis and Toxicity of Tryptamines” Current Neuropharmacology. 13: 26-46. From **p.28** "Alpha-methyltryptamine (AMT) was firstly developed as an **antidepressant agent** called as INDOPAN, in 1960’s by the Upjohn Company and used for a short period of time in the former Soviet Union [20]” From **p.29** "Also alpha-ethyltryptamine (AET) was firstly introduced as an **antidepressant agent** by Upjohn company in 1960s with the name MONASE, but it was withdrawn from the market because of an unacceptable incidence of idiosyncratic agranulocytosis. **AET may induce serotonin neurotoxicity** [26], similar to that of **MDMA** and para-chloroamphetamine (PCA), as reported in studies on rats.", "**The dosage reported by Shulgin, for oral administration, is 100-150 mg. and it seems to be able to fight opiate addiction in anecdotal reports**. “It appears to serve well, with short term dosage regimens, as an effective tool in kicking dependency on opiates” From **p.33 Table 2**. "**AMT** experience... "I got a strong psychedelic experience that lasted about twelve hours, but **an unexpected relief from my chronic depression that lasted for four days**."" From **p.35** "Synthetic 4-substituted tryptamines are orally active and they seem to produce similar effects to those mediated by psilocin." "The 5-substituted tryptamines are more powerful than the unsubstituted molecules, but clinical effects reported are similar among them. Effects reported as “positive” by users of 5-substituted tryptamines include [58]: euphoria, an increasing of energy, libido, concentration and sociability, and **a reduction in fear and anxiety**"