IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: SCHINDLER; Emmanuelle Confirmation No.:

Serial No.: 17/168638 Group No.:

Filing or 371(c) Date: February 5, 2021 Examiner:

Entitled: PSYCHEDELIC TREATMENT FOR HEADACHE DISORDERS

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 (Most references also available at Porta Sophia – the psychedelic prior art library: https://www.portasophia.org/):

1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10.

2. BEUG (1982) "Psilocybin and psilocin levels in twenty species from seven genera of wild mushrooms in the Pacific Northwest, U.S.A." Journal of Ethnopharmacology. 5(3):271-285.

3. McGREENEY (2012) "Cannabinoids and Hallucinogens for Headache" Headache. 53(3):447-458.

4. TARAHAN (2018) "Effects of serotonergic hallucinogen R(−)-2,5-Dimethoxy 4-iodoamphetamine (DOI) on temporal discrimination in mice" FASEB J. 31(S1)1059.

5. SEWELL (2006) "Response of cluster headache to psilocybin and LSD" Neurology. 66(12) 1920-1922.

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. 17/168,638 Pending Claims	References
1. A method of treating headache disorders, the method comprising: administering an effective amount of a composition comprising a psychedelic to an individual in need thereof; and treating the headache disorder.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 1** "Primarily, psilocybin, lysergic acid diethylamide, and related **psychedelic tryptamines were reportedly effective for both prophylactic and acute treatment of cluster headache and migraines**."
2. The method of claim 1, wherein the psychedelic is selected from the group consisting of psilocybin, lysergic acid diethylamide (LSD), mescaline, dimethyltryptamine (DMT), 2,5-dimethoxy-4-iodoamphetamine (DOI), 2,5-dimethoxy-4-bromoamphetamie (DOB), salts thereof, analogs thereof, or homologues thereof.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 1** "Primarily, **psilocybin, lysergic acid diethylamide, and related psychedelic tryptamines** were reportedly **effective for both prophylactic and acute treatment of cluster headache and migraines**." From **p. 6** "Also, for **DMT**, it was suggested that **singular or infrequent** dosage could have potential **long-term beneficial effects on headache disorders: 'Even a single dose, or perhaps a couple, can be a lifelong benefit**.'" 3. McGREENEY (2012) "Cannabinoids and Hallucinogens for Headache" Headache. 53(3):447-458. From **p. 452** "The first comment on **improvement in headache** with hallucinogens is attributed to Prentiss and Morgan, experimenting with peyote (**mescaline**) in 1894." 4. TARAHAN (2018) "Effects of serotonergic hallucinogen R(−)-2,5-Dimethoxy 4-iodoamphetamine (DOI) on temporal discrimination in mice" FASEB. 31(S1)1059. From **p. 1059** "R(−)-**2,5-Dimethoxy-4-iodoamphetamine (DOI)** and other compounds with agonist affinity for serotonergic 5-HT2A receptors are hallucinogenic drugs of abuse, but also have therapeutic potential in numerous neuropsychiatric conditions, including major depressive disorder, post-traumatic stress disorder, and in the **treatment of migraine and cluster headaches**."
3. The method of claim 1, wherein the headache disorder is selected from the group consisting of	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10.

migraine, tension-type headache, cluster headache, and secondary headache disorders.	From **p. 1** "Primarily, psilocybin, lysergic acid diethylamide, and related **psychedelic tryptamines were reportedly effective for both prophylactic and acute treatment of cluster headache and migraines**."
4. The method of claim 1, wherein the method further comprises a step of reducing headache burden by acute treatment of the headache disorder or prevention of the headache disorder.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 1** "Primarily, psilocybin, lysergic acid diethylamide, and related **psychedelic tryptamines were reportedly effective for both prophylactic and acute treatment of cluster headache and migraines**."
5. The method of claim 1, wherein said administering step comprises administering 1-50 mg of psilocybin orally.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 4** "**Psilocybin, or psilocybin-containing mushrooms, was commonly utilized for both migraines and CH**: 'I used magic mushrooms to abort my chronic migraines.'/'I am taking mushrooms for the treatment of cluster headaches.'" From **p. 5** "The data contained a few discussions on various routes for administrating **psilocybin**, some suggested sublingual administration (ground up mushrooms under the tongue), and others preferred to mix the mushrooms with water or juice for **drinking**." From **p. 5** "A benchmark for occasional single doses of psilocybin was around 1 g of dry Psilocybe cubensis but could vary between 0.25 g and as much as 3 g. An ideal dose for one individual could be far too much for another. The preferred dosage varied with the sensitivity of the user and the desired effects: 'You might have to experiment with the dose a bit because what works for one person does not necessarily work for another.' The potency of the material and particular type of mushrooms also called for different dosage: 'Around one gram of dried Cubensis is regularly used for a dose.' P. cubensis was the most common variety, but other species of mushrooms were also discussed: 'With Psilocybe azurescens or **Psilocybe cyanescens, 0.25 gram** should be sufficient.'" 2. BEUG (1982) "Psilocybin and psilocin levels in twenty species from seven genera of wild mushrooms in the Pacific Northwest, U.S.A." Journal of Ethnopharmacology. 5(3):271-285. From **p. 281**

TABLE 1

Psilocybin and psilocin levels in Pacific Northwest mushrooms as quantified by reversed phase HPLC

Species[1] (Figs. 1 - 20)	Date collected[2]	Psilocybin (mg/g dry weight)	Psilocin (mg/g dry weight)
Conocybe cyanopus (Atk.) Kühner	July 12, 1979	9.3	0
Conocybe tenera (Schaeff. ex Fr.) Kühner	Aug. 22, 1978	0	0
Conocybe sp. (near *lactea* (J. Lange) Métrod)	Aug. 13, 1978	0	0
Pholiotina filaris (Fr.) Singer	Oct. 1979	0	0
Panaeolus campanulatus (Fr.) Quél.	Aug. 13, 1978	0	0
	Sept. 4, 1978	0	0
	Mar. 18, 1980	0	0
Panaeolus acuminatus (Sec.) Quél.	Sept. 4, 1978	0	0
	Mar. 18, 1980	0	0
Panaeolus phalaenarum (Fr.) Quél.	July 23, 1978	0	0
	Cultivated	0	0
Psathyrella foenisecii (Fr.) Smith	June 18, 1978	0	0
	Oct. 4, 1978	0	0
Panaeolus semiovatus (Fr.) Lundell & Nanfeldt	June 28, 1978	0	0
	July 12, 1979 (3 collections)	0	0
Panaeolus subbalteatus (Berk. & Br.) Sacc.	July 3, 1978	3.5	0
	Sept. 5, 1978	6.5	0
	Sept. 3, 1979	1.6	0
Gymnopilus ventricosus (Earle) Hesler (generally identified as *G. spectabilis*)	Oct. 15, 1979	0	0
Stropharia aeruginosa (Fr.) Quél.	Oct. 29, 1979	0	0
Psilocybe semilanceata (Fr.) Quél.	Oct. 1979	6.9	0
	Sept. 4, 1978	10.8	0
	Oct. 22, 1979	12.0	0
	Nov. 5, 1979	6.9	0
	Nov. 27, 1979a	8.4	0
	Nov. 27, 1979b	12.8	0
	Nov. 27, 1979c	9.2	0
	Nov. 27, 1979d	6.6	0
	Nov. 27, 1979e	10.9	0
	Nov. 27, 1979f	8.5	0
Caps only	Nov. 27, 1979g	11.1	0
Stems only	Nov. 27, 1979g	6.2	0
Psilocybe cyanescens Wakefield	Oct. 1978a	4.9	1.7
	Oct. 28, 1979	1.5	9.6
	Nov. 2, 1979	8.2	1.3
	Nov. 6, 1979	11.5	7.6

	TABLE 1 *(continued)* **Species[1] (Figs. 1 - 20)** — **Date collected[2]** — **Psilocybin (mg/g dry weight)** — **Psilocin (mg/g dry weight)** *Psilocybe cyanescens* Wakefield — Nov. 7, 1979a — 8.3 — 2.0 Nov. 7, 1979b — 16.8 — 2.8 Nov. 18, 1979a — 14.3 — 2.8 Nov. 18, 1979b — 15.5 — 2.4 Nov. 18, 1979c — 13.6 — 2.3 Nov. 18, 1979d — 11.0 — 2.0 Nov. 18, 1979e — 10.1 — 1.4 Nov. 18, 1979f — 8.7 — 1.8 Nov. 18, 1979g — 9.7 — 2.8 Nov. 19, 1979 — 8.4 — 0.6 *Psilocybe stuntzii* Guzmán & Ott — Sept. 24, 1978 — 0 — 0 Oct. 27, 1979 — 3.6 — 0.6 Oct. 31, 1979 — 0.4 — 0.12 Nov. 13, 1979 — 3.6 — 0.06 *Psilocybe baeocystis* Singer & Smith — Sept. 1979a — 2.04 — 1.43 Sept. 1979b — 1.96 — 1.32 Sept. 1979c — 1.92 — 0.48 Sept. 1979d — 2.04 — 3.07 Sept. 5, 1979 — 8.5 — 5.9 Oct. 1979a — 2.8 — 0.8 Oct. 1979b — 1.5 — 0 *Psilocybe coprophila* (Bull. ex Fr.) Kummer — June 22, 1979 — 0 — 0 *Psilocybe montana* (Pers. ex Fr.) Kummer — Mar. 18, 1980 — 0 — 0 *Psilocybe inquilina* (Fr. ex Fr.) Bres. — Mar. 18, 1980 — 0 — 0 *Psilocybe pelliculosa* (Sm.) Singer & Smith — Oct. 30, 1979 — 7.1 — 0 Oct. 8, 1979 — 4.1 — 0 Nov. 8, 1979 — 1.2 — 0
6. The method of claim 1, wherein said administering step further comprises administering the composition daily, weekly, monthly, or semiannually.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 7** "When using **psilocybin**, LSD, or DMT as an **acute treatment,** it was sometimes said to intensify pain and other symptoms initially, before any mitigating or preventative effects on **CH or migraines** were noticed: 'I thought that the mushrooms hadn't helped and I was back to where I started. But I haven't had a headache since that night.' Psilocybin use was occasionally reported to cause anxiety or panic attacks. On the other hand, these adverse effects were also described as manageable by a more infrequent dosage interval by some of the same users: 'I found that if I **didn't take shrooms more than once a month**, I didn't get anxiety.'" From **p. 8** "Generally, self-treatment was implemented according to one of the dosing regimens. Busting (or the 'clusterbuster' method) is an administration regimen where **psychedelic tryptamines** are used in moderate to medium dosage and strategically timed with the regularly cyclic nature of **CH episodes**: 'The use of psilocybin as a way to cure or manage cluster headaches, a.k.a. busting.' The dosage interval can differ between individuals; one example was **dosing every fifth day**

	during a cluster cycle until the cycle is over**.** Preventive doses are often used preceding a cycle to prohibit the onset of episodes or to reduce the intensity and or frequency of attacks."
7. A method of treating migraine headache, the method comprising: administering an effective amount of a psychedelic to an individual in need thereof; and reducing migraine headache burden.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 1** "Primarily, psilocybin, lysergic acid diethylamide, and related **psychedelic tryptamines were reportedly effective for both prophylactic and acute treatment of** cluster headache and **migraines**."
8. The method of claim 7, wherein the psychedelic is selected from the group consisting of psilocybin, lysergic acid diethylamide (LSD), mescaline, dimethyltryptamine (DMT), 2,5-dimethoxy-4-iodoamphetamine (DOI), 2,5-dimethoxy-4-bromoamphetamie (DOB), salts thereof, analogs thereof, or homologues thereof.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 1** "**Primarily, psilocybin, lysergic acid diethylamide**, and related **psychedelic tryptamines were reportedly effective for both prophylactic and acute treatment of** cluster headache and **migraines**." From **p. 6** "Also, for **DMT**, it was suggested that **singular or infrequent** dosage could have potential **long-term beneficial effects on headache disorders: 'Even a single dose, or perhaps a couple, can be a lifelong benefit.'**" 3. McGREENEY (2012) "Cannabinoids and Hallucinogens for Headache" Headache. 53(3):447-458. From **p. 452** "The first comment on **improvement in headache** with hallucinogens is attributed to Prentiss and Morgan, experimenting with peyote (**mescaline**) in 1894." 4. TARAHAN (2018) "Effects of serotonergic hallucinogen R(−)-2,5-Dimethoxy 4-iodoamphetamine (DOI) on temporal discrimination in mice" FASEB. 31(S1)1059. From **p. 1059** "R(−)-**2,5-Dimethoxy-4-iodoamphetamine (DOI)** and other compounds with agonist affinity for serotonergic 5-HT2A receptors are hallucinogenic drugs of abuse, but also have therapeutic potential in numerous neuropsychiatric conditions, including major depressive disorder, post-traumatic stress disorder, and in the **treatment of migraine and cluster headaches**."
9. The method of claim 7, wherein said administering step further comprises administering a single dose or single pulse treatment of psychedelic to the	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 6** "Exact dosages were mostly not defined regarding DMT, but usually a 'full dose' was reportedly required for therapeutic effects on **migraines** or CH: 'It would seem that a complete breakthrough hit is needed for a cure.' Also, for **DMT**, it was suggested that **singular or infrequent dosage could have potential long-**

individual, and further comprises the step of providing a lasting therapeutic effect.	**term beneficial effects on headache disorders: 'Even a single dose, or perhaps a couple, can be a lifelong benefit.'"** From **p. 8** "Principally, three different approaches or regimens for dosing were reviewed and recommended: the **cyclic** 'busting' (or 'clusterbuster') method, frequent 'microdosing,' or **single** and occasional 'full' doses. Generally, self-treatment was implemented according to one of the dosing regimens. Busting (or the 'clusterbuster' method) is an administration regimen where **psychedelic tryptamines** are used in moderate to medium dosage and strategically timed with the regularly cyclic nature of CH episodes: 'The use of psilocybin as a way to cure or manage cluster headaches, a.k.a. busting.' The dosage interval can differ between individuals; one example was dosing every fifth day during a cluster cycle until the cycle is over. Preventive doses are often used preceding a cycle to prohibit the onset of episodes or to reduce the intensity and or frequency of attacks."
10. The method of claim 7, wherein said administering step further comprises administering 1-50 mg of psilocybin orally.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 4** "**Psilocybin, or psilocybin-containing mushrooms, was commonly utilized for both migraines and CH**: 'I used magic mushrooms to abort my chronic migraines.'/'I am taking mushrooms for the treatment of cluster headaches.'" From **p. 5** "The data contained a few discussions on various routes for administrating **psilocybin**, some suggested sublingual administration (ground up mushrooms under the tongue), and others preferred to mix the mushrooms with water or juice for **drinking**." From **p. 5** "A benchmark for occasional single doses of psilocybin was around 1 g of dry Psilocybe cubensis but could vary between 0.25 g and as much as 3 g. An ideal dose for one individual could be far too much for another. The preferred dosage varied with the sensitivity of the user and the desired effects: 'You might have to experiment with the dose a bit because what works for one person does not necessarily work for another.' The potency of the material and particular type of mushrooms also called for different dosage: 'Around one gram of dried Cubensis is regularly used for a dose.' P. cubensis was the most common variety, but other species of mushrooms were also discussed: 'With Psilocybe azurescens or **Psilocybe cyanescens, 0.25 gram** should be sufficient.'" 2. BEUG (1982) "Psilocybin and psilocin levels in twenty species from seven genera of wild mushrooms in the Pacific Northwest, U.S.A." Journal of Ethnopharmacology. 5(3):271-285. From **p. 281**

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	Sept. 4, 1978	0	0
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Panaeolus acuminatus (Sec.) Quél.	Sept. 4, 1978	0	0
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Panaeolus phalaenarum (Fr.) Quél.	July 23, 1978	0	0
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Psathyrella foenisecii (Fr.) Smith	June 18, 1978	0	0
	Oct. 4, 1978	0	0
Panaeolus semiovatus (Fr.) Lundell & Nanfeldt	June 28, 1978	0	0
	July 12, 1979 (3 collections)	0	0
Panaeolus subbalteatus (Berk. & Br.) Sacc.	July 3, 1978	3.5	0
	Sept. 5, 1978	6.5	0
	Sept. 3, 1979	1.6	0
Gymnopilus ventricosus (Earle) Hesler (generally identified as *G. spectabilis*)	Oct. 15, 1979	0	0
Stropharia aeruginosa (Fr.) Quél.	Oct. 29, 1979	0	0
Psilocybe semilanceata (Fr.) Quél.	Oct. 1979	6.9	0
	Sept. 4, 1978	10.8	0
	Oct. 22, 1979	12.0	0
	Nov. 5, 1979	6.9	0
	Nov. 27, 1979a	8.4	0
	Nov. 27, 1979b	12.8	0
	Nov. 27, 1979c	9.2	0
	Nov. 27, 1979d	6.6	0
	Nov. 27, 1979e	10.9	0
	Nov. 27, 1979f	8.5	0
Caps only	Nov. 27, 1979g	11.1	0
Stems only	Nov. 27, 1979g	6.2	0
Psilocybe cyanescens Wakefield	Oct. 1978a	4.9	1.7
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	TABLE 1 *(continued)* Species[1] (Figs. 1 - 20) / Date collected[2] / Psilocybin (mg/g dry weight) / Psilocin (mg/g dry weight) *Psilocybe cyanescens* Wakefield: Nov. 7, 1979a — 8.3 — 2.0; Nov. 7, 1979b — 16.8 — 2.8; Nov. 18, 1979a — 14.3 — 2.8; Nov. 18, 1979b — 15.5 — 2.4; Nov. 18, 1979c — 13.6 — 2.3; Nov. 18, 1979d — 11.0 — 2.0; Nov. 18, 1979e — 10.1 — 1.4; Nov. 18, 1979f — 8.7 — 1.8; Nov. 18, 1979g — 9.7 — 2.8; Nov. 19, 1979 — 8.4 — 0.6 *Psilocybe stuntzii* Guzmán & Ott: Sept. 24, 1978 — 0 — 0; Oct. 27, 1979 — 3.6 — 0.6; Oct. 31, 1979 — 0.4 — 0.12; Nov. 13, 1979 — 3.6 — 0.06 *Psilocybe baeocystis* Singer & Smith: Sept. 1979a — 2.04 — 1.43; Sept. 1979b — 1.96 — 1.32; Sept. 1979c — 1.92 — 0.48; Sept. 1979d — 2.04 — 3.07; Sept. 5, 1979 — 8.5 — 5.9; Oct. 1979a — 2.8 — 0.8; Oct. 1979b — 1.5 — 0 *Psilocybe coprophila* (Bull. ex Fr.) Kummer: June 22, 1979 — 0 — 0 *Psilocybe montana* (Pers. ex Fr.) Kummer: Mar. 18, 1980 — 0 — 0 *Psilocybe inquilina* (Fr. ex Fr.) Bres.: Mar. 18, 1980 — 0 — 0 *Psilocybe pelliculosa* (Sm.) Singer & Smith: Oct. 30, 1979 — 7.1 — 0; Oct. 8, 1979 — 4.1 — 0; Nov. 8, 1979 — 1.2 — 0
11. The method of claim 10, wherein said administering step further comprises administering 0.143 mg/kg of psilocybin orally.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 4** "**Psilocybin, or psilocybin-containing mushrooms, was commonly utilized for both migraines and CH**: "I used magic mushrooms to abort my chronic migraines."/"I am taking mushrooms for the treatment of cluster headaches."" From **p. 5** "The data contained a few discussions on various routes for administrating **psilocybin**, some suggested sublingual administration (ground up mushrooms under the tongue), and others preferred to mix the mushrooms with water or juice for **drinking**." From **p. 5** "A benchmark for occasional single doses of psilocybin was around 1 g of dry Psilocybe cubensis but could vary between 0.25 g and as much as 3 g. An ideal dose for one individual could be far too much for another. The preferred dosage varied with the sensitivity of the user and the desired effects: 'You might have to experiment with the dose a bit because what works for one person does not necessarily work for another.' The potency of the material and particular type of

	mushrooms also called for different dosage: ‘Around one gram of dried Cubensis is regularly used for a dose.’ P. cubensis was the most common variety, but other species of mushrooms were also discussed: ‘With Psilocybe azurescens or **Psilocybe cyanescens, 0.25 gram** should be sufficient.’” 2. BEUG (1982) “Psilocybin and psilocin levels in twenty species from seven genera of wild mushrooms in the Pacific Northwest, U.S.A.” Journal of Ethnopharmacology. 5(3):271-285. From **p. 281**

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	Oct. 22, 1979	12.0	0
	Nov. 5, 1979	6.9	0
	Nov. 27, 1979a	8.4	0
	Nov. 27, 1979b	12.8	0
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12. The method of claim 7, further comprising the step of administering a follow up dose of the psychedelic at a time selected from the group consisting of weekly, monthly, and yearly.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 7** "When using **psilocybin, LSD, or DMT as an acute treatment,** it was sometimes said to intensify pain and other symptoms initially, before any mitigating or preventative effects on CH or **migraines** were noticed: 'I thought that the mushrooms hadn't helped and I was back to where I started. But I haven't had a headache since that night.' Psilocybin use was occasionally reported to cause anxiety or panic attacks. On the other hand, these adverse effects were also described as manageable by a more infrequent dosage interval by some of the same users: 'I found that if I **didn't take shrooms more than once a month**, I didn't get anxiety.'" From **p. 8** "Generally, self-treatment was implemented according to one of the dosing regimens. Busting (or the 'clusterbuster' method) is an administration regimen where **psychedelic tryptamines** are used in moderate to medium dosage and strategically timed with the regularly cyclic nature of CH episodes: 'The use of psilocybin as a way to cure or manage cluster headaches, a.k.a. busting.' **The dosage interval can differ between individuals; one example was dosing every**

	fifth day during a cluster cycle until the cycle is over. Preventive doses are often used preceding a cycle to prohibit the onset of episodes or to reduce the intensity and or frequency of attacks."
13. The method of claim 7, wherein said reducing step further comprises a step selected from the group consisting of reducing the number of migraine days per week, reducing pain severity, reducing migraine abortive use, reducing attack-related functional impairment, and increasing the time between migraine attacks in the individual.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 7** "Self-treatment with **psychedelic tryptamines**, primarily LSD and psilocybin, was reported to provide a significant **lessening of the frequency and intensity of attacks** in many cases of both CH and **migraines**."
14. The method of claim 7, wherein said reducing step further comprises a step selected from the group consisting of acutely treating migraine headache and preventing migraine headache.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 1** "Primarily, psilocybin, lysergic acid diethylamide, and related **psychedelic tryptamines were reportedly effective for both prophylactic and acute treatment of** cluster headache and **migraines**."
15. A method of treating cluster headache, the method comprising: administering an effective amount of a psychedelic to an individual in need thereof; and reducing cluster headache burden.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 1** "Primarily, psilocybin, lysergic acid diethylamide, and related **psychedelic tryptamines were reportedly effective for both prophylactic and acute treatment of cluster headache** and migraines."
16. The method of claim 15, wherein the psychedelic is selected from the group consisting of psilocybin, lysergic	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10.

acid diethylamide (LSD), mescaline, dimethyltryptamine (DMT), 2,5-dimethoxy-4-iodoamphetamine (DOI), 2,5-dimethoxy-4-bromoamphetamie (DOB), salts thereof, analogs thereof, or homologues thereof.	From **p. 1** "Primarily, **psilocybin, lysergic acid diethylamide**, and related **psychedelic tryptamines were reportedly effective for both prophylactic and acute treatment of cluster headache** and migraines." From **p. 6** "Also, for **DMT**, it was suggested that **singular or infrequent** dosage could have potential **long-term beneficial effects on headache disorders: 'Even a single dose, or perhaps a couple, can be a lifelong benefit**.'" 3. McGREENEY (2012) "Cannabinoids and Hallucinogens for Headache" Headache. 53(3):447-458. From **p. 452** "The first comment on **improvement in headache** with hallucinogens is attributed to Prentiss and Morgan, experimenting with peyote (**mescaline**) in 1894." 4. TARAHAN (2018) "Effects of serotonergic hallucinogen R(−)-2,5-Dimethoxy 4-iodoamphetamine (DOI) on temporal discrimination in mice" FASEB. 31(S1)1059. From **p. 1059** "R(−)-**2,5-Dimethoxy-4-iodoamphetamine (DOI)** and other compounds with agonist affinity for serotonergic 5-HT2A receptors are hallucinogenic drugs of abuse, but also have therapeutic potential in numerous neuropsychiatric conditions, including major depressive disorder, post-traumatic stress disorder, and in the **treatment of migraine and cluster headaches**."
17. The method of claim 15, wherein said administering step further comprises administering the psychedelic in a three dose pulse regimen with a 3-7 day separation between doses.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 8** "Generally, self-treatment was implemented according to one of the dosing regimens. Busting (or the 'clusterbuster' method) is an administration regimen where **psychedelic tryptamines** are used in moderate to medium dosage and strategically timed with the regularly cyclic nature of **CH episodes**: 'The use of psilocybin as a way to cure or manage cluster headaches, a.k.a. busting.' The dosage interval can differ between individuals; one example was **dosing every fifth day during a cluster cycle** until the cycle is over**.** Preventive doses are often used preceding a cycle to prohibit the onset of episodes or to reduce the intensity and or frequency of attacks." 5. SEWELL (2006) "Response of cluster headache to psilocybin and LSD" Neurology. 66(12) 1920-1922. From p. 1920: "Our results are interesting for three reasons. First, no other medication, to our knowledge, has been reported to terminate a cluster period. Second, unlike other ergot-based medications, which must be taken daily, a single dose of LSD was described as sufficient to induce remission of a **cluster period**, and **psilocybin** rarely required more than **three doses**."
18. The method of claim 17, further comprising the step of administering a second round of the	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10.

three dose pulse regimen at a later time.	From **p. 8** "Generally, self-treatment was implemented according to one of the dosing regimens. Busting (or the 'clusterbuster' method) is an administration regimen where **psychedelic tryptamines** are used in moderate to medium dosage and strategically timed with the regularly cyclic nature of CH episodes: 'The use of psilocybin as a way to cure or manage cluster headaches, a.k.a. busting.' The dosage interval can differ between individuals; one example was **dosing every fifth day during a cluster cycle until the cycle is over.** Preventive doses are often used preceding a cycle to prohibit the onset of episodes or to reduce the intensity and or frequency of attacks." 5. SEWELL (2006) "Response of cluster headache to psilocybin and LSD" Neurology. 66(12) 1920-1922. From p. 1920: "Our results are interesting for three reasons. First, no other medication, to our knowledge, has been reported to terminate a cluster period. Second, unlike other ergot-based medications, which must be taken daily, a single dose of LSD was described as sufficient to induce remission of a **cluster period**, and **psilocybin** rarely required more than **three doses**."
19. The method of claim 15, wherein said administering step further comprises administering 1-50 mg of psilocybin orally.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 4** "**Psilocybin, or psilocybin-containing mushrooms, was commonly utilized for both migraines and CH**: 'I used magic mushrooms to abort my chronic migraines.'/'I am taking mushrooms for the treatment of cluster headaches.'" From **p. 5** "The data contained a few discussions on various routes for administrating **psilocybin**, some suggested sublingual administration (ground up mushrooms under the tongue), and others preferred to mix the mushrooms with water or juice for **drinking**." From **p. 5** "A benchmark for occasional single doses of psilocybin was around 1 g of dry Psilocybe cubensis but could vary between 0.25 g and as much as 3 g. An ideal dose for one individual could be far too much for another. The preferred dosage varied with the sensitivity of the user and the desired effects: 'You might have to experiment with the dose a bit because what works for one person does not necessarily work for another.' The potency of the material and particular type of mushrooms also called for different dosage: 'Around one gram of dried Cubensis is regularly used for a dose.' P. cubensis was the most common variety, but other species of mushrooms were also discussed: 'With Psilocybe azurescens or **Psilocybe cyanescens, 0.25 gram** should be sufficient.'" 2. BEUG (1982) "Psilocybin and psilocin levels in twenty species from seven genera of wild mushrooms in the Pacific Northwest, U.S.A." Journal of Ethnopharmacology. 5(3):271-285. From **p. 281**

TABLE 1

Psilocybin and psilocin levels in Pacific Northwest mushrooms as quantified by reversed phase HPLC

Species[1] (Figs. 1 - 20)	Date collected[2]	Psilocybin (mg/g dry weight)	Psilocin (mg/g dry weight)
Conocybe cyanopus (Atk.) Kühner	July 12, 1979	9.3	0
Conocybe tenera (Schaeff. ex Fr.) Kühner	Aug. 22, 1978	0	0
Conocybe sp. (near *lactea* (J. Lange) Métrod)	Aug. 13, 1978	0	0
Pholiotina filaris (Fr.) Singer	Oct. 1979	0	0
Panaeolus campanulatus (Fr.) Quél.	Aug. 13, 1978	0	0
	Sept. 4, 1978	0	0
	Mar. 18, 1980	0	0
Panaeolus acuminatus (Sec.) Quél.	Sept. 4, 1978	0	0
	Mar. 18, 1980	0	0
Panaeolus phalaenarum (Fr.) Quél.	July 23, 1978	0	0
	Cultivated	0	0
Psathyrella foenisecii (Fr.) Smith	June 18, 1978	0	0
	Oct. 4, 1978	0	0
Panaeolus semiovatus (Fr.) Lundell & Nanfeldt	June 28, 1978	0	0
	July 12, 1979 (3 collections)	0	0
Panaeolus subbalteatus (Berk. & Br.) Sacc.	July 3, 1978	3.5	0
	Sept. 5, 1978	6.5	0
	Sept. 3, 1979	1.6	0
Gymnopilus ventricosus (Earle) Hesler (generally identified as *G. spectabilis*)	Oct. 15, 1979	0	0
Stropharia aeruginosa (Fr.) Quél.	Oct. 29, 1979	0	0
Psilocybe semilanceata (Fr.) Quél.	Oct. 1979	6.9	0
	Sept. 4, 1978	10.8	0
	Oct. 22, 1979	12.0	0
	Nov. 5, 1979	6.9	0
	Nov. 27, 1979a	8.4	0
	Nov. 27, 1979b	12.8	0
	Nov. 27, 1979c	9.2	0
	Nov. 27, 1979d	6.6	0
	Nov. 27, 1979e	10.9	0
	Nov. 27, 1979f	8.5	0
Caps only	Nov. 27, 1979g	11.1	0
Stems only	Nov. 27, 1979g	6.2	0
Psilocybe cyanescens Wakefield	Oct. 1978a	4.9	1.7
	Oct. 28, 1979	1.5	9.6
	Nov. 2, 1979	8.2	1.3
	Nov. 6, 1979	11.5	7.6

	TABLE 1 *(continued)* Species[1] (Figs. 1 - 20) / Date collected[2] / Psilocybin (mg/g dry weight) / Psilocin (mg/g dry weight) *Psilocybe cyanescens* Wakefield: Nov. 7, 1979a — 8.3 — 2.0; Nov. 7, 1979b — 16.8 — 2.8; Nov. 18, 1979a — 14.3 — 2.8; Nov. 18, 1979b — 15.5 — 2.4; Nov. 18, 1979c — 13.6 — 2.3; Nov. 18, 1979d — 11.0 — 2.0; Nov. 18, 1979e — 10.1 — 1.4; Nov. 18, 1979f — 8.7 — 1.8; Nov. 18, 1979g — 9.7 — 2.8; Nov. 19, 1979 — 8.4 — 0.6 *Psilocybe stuntzii* Guzmán & Ott: Sept. 24, 1978 — 0 — 0; Oct. 27, 1979 — 3.6 — 0.6; Oct. 31, 1979 — 0.4 — 0.12; Nov. 13, 1979 — 3.6 — 0.06 *Psilocybe baeocystis* Singer & Smith: Sept. 1979a — 2.04 — 1.43; Sept. 1979b — 1.96 — 1.32; Sept. 1979c — 1.92 — 0.48; Sept. 1979d — 2.04 — 3.07; Sept. 5, 1979 — 8.5 — 5.9; Oct. 1979a — 2.8 — 0.8; Oct. 1979b — 1.5 — 0 *Psilocybe coprophila* (Bull. ex Fr.) Kummer: June 22, 1979 — 0 — 0 *Psilocybe montana* (Pers. ex Fr.) Kummer: Mar. 18, 1980 — 0 — 0 *Psilocybe inquilina* (Fr. ex Fr.) Bres.: Mar. 18, 1980 — 0 — 0 *Psilocybe pelliculosa* (Sm.) Singer & Smith: Oct. 30, 1979 — 7.1 — 0; Oct. 8, 1979 — 4.1 — 0; Nov. 8, 1979 — 1.2 — 0
20. The method of claim 19, wherein said administering step further comprises administering 0.143 mg/kg of the psilocybin orally.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 4** "**Psilocybin, or psilocybin-containing mushrooms, was commonly utilized for both migraines and CH**: 'I used magic mushrooms to abort my chronic migraines.'/'I am taking mushrooms for the treatment of cluster headaches.'" From **p. 5** "The data contained a few discussions on various routes for administrating **psilocybin**, some suggested sublingual administration (ground up mushrooms under the tongue), and others preferred to mix the mushrooms with water or juice for **drinking**." From **p. 5** "A benchmark for occasional single doses of psilocybin was around 1 g of dry Psilocybe cubensis but could vary between 0.25 g and as much as 3 g. An ideal dose for one individual could be far too much for another. The preferred dosage varied with the sensitivity of the user and the desired effects: 'You might have to experiment with the dose a bit because what works for one person does not necessarily work for another.' The potency of the material and particular type of

	mushrooms also called for different dosage: ‘Around one gram of dried Cubensis is regularly used for a dose.’ P. cubensis was the most common variety, but other species of mushrooms were also discussed: ‘With Psilocybe azurescens or **Psilocybe cyanescens, 0.25 gram** should be sufficient.’” 2. BEUG (1982) “Psilocybin and psilocin levels in twenty species from seven genera of wild mushrooms in the Pacific Northwest, U.S.A.” Journal of Ethnopharmacology. 5(3):271-285. From **p. 281**

TABLE 1

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Species[1] (Figs. 1 - 20)	Date collected[2]	Psilocybin (mg/g dry weight)	Psilocin (mg/g dry weight)
Conocybe cyanopus (Atk.) Kühner	July 12, 1979	9.3	0
Conocybe tenera (Schaeff. ex Fr.) Kühner	Aug. 22, 1978	0	0
Conocybe sp. (near *lactea* (J. Lange) Métrod)	Aug. 13, 1978	0	0
Pholiotina filaris (Fr.) Singer	Oct. 1979	0	0
Panaeolus campanulatus	Aug. 13, 1978	0	0
(Fr.) Quél.	Sept. 4, 1978	0	0
	Mar. 18, 1980	0	0
Panaeolus acuminatus	Sept. 4, 1978	0	0
(Sec.) Quél.	Mar. 18, 1980	0	0
Panaeolus phalaenarum	July 23, 1978	0	0
(Fr.) Quél.	Cultivated	0	0
Psathyrella foenisecii	June 18, 1978	0	0
(Fr.) Smith	Oct. 4, 1978	0	0
Panaeolus semiovatus	June 28, 1978	0	0
(Fr.) Lundell & Nan-	July 12, 1979	0	0
feldt	(3 collections)		
Panaeolus subbalteatus	July 3, 1978	3.5	0
(Berk. & Br.) Sacc.	Sept. 5, 1978	6.5	0
	Sept. 3, 1979	1.6	0
Gymnopilus ventricosus (Earle) Hesler (generally identified as *G. spectabilis*)	Oct. 15, 1979	0	0
Stropharia aeruginosa (Fr.) Quél.	Oct. 29, 1979	0	0
Psilocybe semilanceata	Oct. 1979	6.9	0
(Fr.) Quél.	Sept. 4, 1978	10.8	0
	Oct. 22, 1979	12.0	0
	Nov. 5, 1979	6.9	0
	Nov. 27, 1979a	8.4	0
	Nov. 27, 1979b	12.8	0
	Nov. 27, 1979c	9.2	0
	Nov. 27, 1979d	6.6	0
	Nov. 27, 1979e	10.9	0
	Nov. 27, 1979f	8.5	0
Caps only	Nov. 27, 1979g	11.1	0
Stems only	Nov. 27, 1979g	6.2	0
Psilocybe cyanescens	Oct. 1978a	4.9	1.7
Wakefield	Oct. 28, 1979	1.5	9.6
	Nov. 2, 1979	8.2	1.3
	Nov. 6, 1979	11.5	7.6

	TABLE 1 *(continued)* Species[1] (Figs. 1 - 20) / Date collected[2] / Psilocybin (mg/g dry weight) / Psilocin (mg/g dry weight) *Psilocybe cyanescens* Wakefield: Nov. 7, 1979a — 8.3 — 2.0; Nov. 7, 1979b — 16.8 — 2.8; Nov. 18, 1979a — 14.3 — 2.8; Nov. 18, 1979b — 15.5 — 2.4; Nov. 18, 1979c — 13.6 — 2.3; Nov. 18, 1979d — 11.0 — 2.0; Nov. 18, 1979e — 10.1 — 1.4; Nov. 18, 1979f — 8.7 — 1.8; Nov. 18, 1979g — 9.7 — 2.8; Nov. 19, 1979 — 8.4 — 0.6 *Psilocybe stuntzii* Guzmán & Ott: Sept. 24, 1978 — 0 — 0; Oct. 27, 1979 — 3.6 — 0.6; Oct. 31, 1979 — 0.4 — 0.12; Nov. 13, 1979 — 3.6 — 0.06 *Psilocybe baeocystis* Singer & Smith: Sept. 1979a — 2.04 — 1.43; Sept. 1979b — 1.96 — 1.32; Sept. 1979c — 1.92 — 0.48; Sept. 1979d — 2.04 — 3.07; Sept. 5, 1979 — 8.5 — 5.9; Oct. 1979a — 2.8 — 0.8; Oct. 1979b — 1.5 — 0 *Psilocybe coprophila* (Bull. ex Fr.) Kummer: June 22, 1979 — 0 — 0 *Psilocybe montana* (Pers. ex Fr.) Kummer: Mar. 18, 1980 — 0 — 0 *Psilocybe inquilina* (Fr. ex Fr.) Bres.: Mar. 18, 1980 — 0 — 0 *Psilocybe pelliculosa* (Sm.) Singer & Smith: Oct. 30, 1979 — 7.1 — 0; Oct. 8, 1979 — 4.1 — 0; Nov. 8, 1979 — 1.2 — 0
21. The method of claim 15, wherein said administering step further comprises administering the composition daily, weekly, monthly, or semiannually.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 7** "When using **psilocybin, LSD, or DMT as an acute treatment,** it was sometimes said to intensify pain and other symptoms initially, before any mitigating or preventative effects on **CH** or migraines were noticed: 'I thought that the mushrooms hadn't helped and I was back to where I started. But I haven't had a headache since that night.' Psilocybin use was occasionally reported to cause anxiety or panic attacks. On the other hand, these adverse effects were also described as manageable by a more infrequent dosage interval by some of the same users: 'I found that if I **didn't take shrooms more than once a month**, I didn't get anxiety.'" From **p. 8** "Generally, self-treatment was implemented according to one of the dosing regimens. Busting (or the 'clusterbuster' method) is an administration regimen where **psychedelic tryptamines** are used in moderate to medium dosage and strategically timed with the regularly cyclic nature of **CH episodes**: 'The use of psilocybin as a way to cure or manage cluster headaches, a.k.a. busting.' The dosage interval can differ between individuals; one example was **dosing every fifth day**

	during a cluster cycle until the cycle is over**.** Preventive doses are often used preceding a cycle to prohibit the onset of episodes or to reduce the intensity and or frequency of attacks."
22. The method of claim 15, wherein said reducing step further comprises reducing the number of weekly cluster attacks in the individual.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 1** "Primarily, psilocybin, lysergic acid diethylamide, and related **psychedelic tryptamines were reportedly effective for both prophylactic and acute treatment of cluster headache** and migraines." From **p. 8** "Generally, self-treatment was implemented according to one of the dosing regimens. Busting (or the 'clusterbuster' method) is an administration regimen where **psychedelic tryptamines are used in moderate to medium dosage and strategically timed with the regularly cyclic nature of CH episodes**: 'The use of psilocybin as a way to cure or manage cluster headaches, a.k.a. busting.' The dosage interval can differ between individuals; one example was dosing every fifth day during a cluster cycle until the cycle is over**.** Preventive doses are often used preceding a cycle to prohibit the onset of episodes or to **reduce the intensity and or frequency of attacks**."
23. The method of claim 15, wherein said reducing step further comprises a step selected from the group consisting of acutely treating cluster headache and preventing cluster headaches.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 1** "Primarily, psilocybin, lysergic acid diethylamide, and related **psychedelic tryptamines were reportedly effective for both prophylactic and acute treatment of cluster headache** and migraines." From **p. 8** "Generally, self-treatment was implemented according to one of the dosing regimens. Busting (or the 'clusterbuster' method) is an administration regimen where **psychedelic tryptamines are used in moderate to medium dosage and strategically timed with the regularly cyclic nature of CH episodes**: 'The use of psilocybin as a way to cure or manage cluster headaches, a.k.a. busting.' The dosage interval can differ between individuals; one example was dosing every fifth day during a cluster cycle until the cycle is over**. Preventive doses** are often used preceding a cycle to prohibit the onset of episodes or to **reduce the intensity and or frequency of attacks**."
24. The method of treating headache disorders, the method comprising: administering a single treatment of a psychedelic to an individual in need thereof; and providing a long term effect in preventing headaches.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 6** "Also, for **DMT**, it was suggested that **singular** or infrequent dosage could have potential **long-term beneficial effects on headache disorders: 'Even a single dose, or perhaps a couple, can be a lifelong benefit**.'"

25. The method of claim 24, wherein the treatment is selected from the group consisting of a single dose and a single pulse regimen.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 1** "Primarily, psilocybin, lysergic acid diethylamide, and related **psychedelic tryptamines were reportedly effective for both prophylactic and acute treatment of cluster headache and migraines**." From **p. 6** "Also, for **DMT**, it was suggested that **singular or infrequent** dosage could have potential **long-term beneficial effects on headache disorders: 'Even a single dose, or perhaps a couple, can be a lifelong benefit**.'"
26. The method of claim 24, wherein the headache disorder is selected from the group consisting of migraine and cluster headache.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 1** "Primarily, psilocybin, lysergic acid diethylamide, and related **psychedelic tryptamines were reportedly effective for both prophylactic and acute treatment of cluster headache and migraines**." From **p. 6** "Also, for **DMT**, it was suggested that **singular or infrequent** dosage could have potential **long-term beneficial effects on headache disorders: 'Even a single dose, or perhaps a couple, can be a lifelong benefit**.'"
27. The method of claim 24, wherein the psychedelic is selected from the group consisting of psilocybin, lysergic acid diethylamide (LSD), mescaline, dimethyltryptamine (DMT), 2,5-dimethoxy-4-iodoamphetamine (DOI), 2,5-dimethoxy-4-bromoamphetamie (DOB), salts thereof, analogs thereof, or homologues thereof.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 1** "Primarily, **psilocybin, lysergic acid diethylamide**, and related **psychedelic tryptamines were reportedly effective for both prophylactic and acute treatment of cluster headache and migraines**." From **p. 6** "Also, for **DMT**, it was suggested that **singular or infrequent** dosage could have potential **long-term beneficial effects on headache disorders: 'Even a single dose, or perhaps a couple, can be a lifelong benefit**.'" 3. McGREENEY (2012) "Cannabinoids and Hallucinogens for Headache" Headache. 53(3):447-458. From **p. 452** "The first comment on **improvement in headache** with hallucinogens is attributed to Prentiss and Morgan, experimenting with peyote (**mescaline**) in 1894." 4. TARAHAN (2018) "Effects of serotonergic hallucinogen R(−)-2,5-Dimethoxy 4-iodoamphetamine (DOI) on temporal discrimination in mice" FASEB. 31(S1)1059. From **p. 1059** "R(−)-**2,5-Dimethoxy-4-iodoamphetamine (DOI)** and other compounds with agonist affinity for serotonergic 5-HT2A receptors are hallucinogenic drugs of abuse, but also have therapeutic potential in numerous neuropsychiatric conditions, including major depressive disorder, post-traumatic stress disorder, and in the **treatment of migraine and cluster headaches**."

28. The method of claim 24, wherein said administering step further comprises administering 1-50 mg of psilocybin orally.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 4** "**Psilocybin, or psilocybin-containing mushrooms, was commonly utilized for both migraines and CH**: 'I used magic mushrooms to abort my chronic migraines.'/ 'I am taking mushrooms for the treatment of cluster headaches.'" From **p. 5** "The data contained a few discussions on various routes for administrating **psilocybin**, some suggested sublingual administration (ground up mushrooms under the tongue), and others preferred to mix the mushrooms with water or juice for **drinking**." From **p. 5** "A benchmark for occasional single doses of psilocybin was around 1 g of dry Psilocybe cubensis but could vary between 0.25 g and as much as 3 g. An ideal dose for one individual could be far too much for another. The preferred dosage varied with the sensitivity of the user and the desired effects: 'You might have to experiment with the dose a bit because what works for one person does not necessarily work for another.' The potency of the material and particular type of mushrooms also called for different dosage: 'Around one gram of dried Cubensis is regularly used for a dose.' P. cubensis was the most common variety, but other species of mushrooms were also discussed: 'With Psilocybe azurescens or **Psilocybe cyanescens, 0.25 gram** should be sufficient.'" From **p. 6** "Those using the 'busting method' reported both acute and preventive treatment results, although it was described as crucial to follow a cyclic dosage scheme to obtain **long-term results**. Relapses were reported when the dosing regimen was not followed consistently: 'Mostly pain-free, except for when I did not take my proper preventative dose.' The busting method was reportedly effective with LSD, **psilocybin mushrooms**, and various kinds of LSA containing seeds." 2. BEUG (1982) "Psilocybin and psilocin levels in twenty species from seven genera of wild mushrooms in the Pacific Northwest, U.S.A." Journal of Ethnopharmacology. 5(3):271-285. From **p. 281**

TABLE 1

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Pholiotina filaris (Fr.) Singer	Oct. 1979	0	0
Panaeolus campanulatus (Fr.) Quél.	Aug. 13, 1978	0	0
	Sept. 4, 1978	0	0
	Mar. 18, 1980	0	0
Panaeolus acuminatus (Sec.) Quél.	Sept. 4, 1978	0	0
	Mar. 18, 1980	0	0
Panaeolus phalaenarum (Fr.) Quél.	July 23, 1978	0	0
	Cultivated	0	0
Psathyrella foenisecii (Fr.) Smith	June 18, 1978	0	0
	Oct. 4, 1978	0	0
Panaeolus semiovatus (Fr.) Lundell & Nanfeldt	June 28, 1978	0	0
	July 12, 1979 (3 collections)	0	0
Panaeolus subbalteatus (Berk. & Br.) Sacc.	July 3, 1978	3.5	0
	Sept. 5, 1978	6.5	0
	Sept. 3, 1979	1.6	0
Gymnopilus ventricosus (Earle) Hesler (generally identified as *G. spectabilis*)	Oct. 15, 1979	0	0
Stropharia aeruginosa (Fr.) Quél.	Oct. 29, 1979	0	0
Psilocybe semilanceata (Fr.) Quél.	Oct. 1979	6.9	0
	Sept. 4, 1978	10.8	0
	Oct. 22, 1979	12.0	0
	Nov. 5, 1979	6.9	0
	Nov. 27, 1979a	8.4	0
	Nov. 27, 1979b	12.8	0
	Nov. 27, 1979c	9.2	0
	Nov. 27, 1979d	6.6	0
	Nov. 27, 1979e	10.9	0
	Nov. 27, 1979f	8.5	0
Caps only	Nov. 27, 1979g	11.1	0
Stems only	Nov. 27, 1979g	6.2	0
Psilocybe cyanescens Wakefield	Oct. 1978a	4.9	1.7
	Oct. 28, 1979	1.5	9.6
	Nov. 2, 1979	8.2	1.3
	Nov. 6, 1979	11.5	7.6

	TABLE 1 *(continued)* Species[1] (Figs. 1 - 20) / Date collected[2] / Psilocybin (mg/g dry weight) / Psilocin (mg/g dry weight) *Psilocybe cyanescens* Wakefield: Nov. 7, 1979a — 8.3 — 2.0; Nov. 7, 1979b — 16.8 — 2.8; Nov. 18, 1979a — 14.3 — 2.8; Nov. 18, 1979b — 15.5 — 2.4; Nov. 18, 1979c — 13.6 — 2.3; Nov. 18, 1979d — 11.0 — 2.0; Nov. 18, 1979e — 10.1 — 1.4; Nov. 18, 1979f — 8.7 — 1.8; Nov. 18, 1979g — 9.7 — 2.8; Nov. 19, 1979 — 8.4 — 0.6 *Psilocybe stuntzii* Guzmán & Ott: Sept. 24, 1978 — 0 — 0; Oct. 27, 1979 — 3.6 — 0.6; Oct. 31, 1979 — 0.4 — 0.12; Nov. 13, 1979 — 3.6 — 0.06 *Psilocybe baeocystis* Singer & Smith: Sept. 1979a — 2.04 — 1.43; Sept. 1979b — 1.96 — 1.32; Sept. 1979c — 1.92 — 0.48; Sept. 1979d — 2.04 — 3.07; Sept. 5, 1979 — 8.5 — 5.9; Oct. 1979a — 2.8 — 0.8; Oct. 1979b — 1.5 — 0 *Psilocybe coprophila* (Bull. ex Fr.) Kummer: June 22, 1979 — 0 — 0 *Psilocybe montana* (Pers. ex Fr.) Kummer: Mar. 18, 1980 — 0 — 0 *Psilocybe inquilina* (Fr. ex Fr.) Bres.: Mar. 18, 1980 — 0 — 0 *Psilocybe pelliculosa* (Sm.) Singer & Smith: Oct. 30, 1979 — 7.1 — 0; Oct. 8, 1979 — 4.1 — 0; Nov. 8, 1979 — 1.2 — 0
29. The method of claim 28, wherein said administering step further comprises administering 0.143 mg/kg of the psilocybin orally.	1. ANDERSSON (2017) "Psychoactive substances as a last resort—a qualitative study of self-treatment of migraine and cluster headaches" Harm Reduction Journal. 14(1):1-10. From **p. 4** "**Psilocybin, or psilocybin-containing mushrooms, was commonly utilized for both migraines and CH**: 'I used magic mushrooms to abort my chronic migraines.'/'I am taking mushrooms for the treatment of cluster headaches.'" From **p. 5** "The data contained a few discussions on various routes for administrating **psilocybin**, some suggested sublingual administration (ground up mushrooms under the tongue), and others preferred to mix the mushrooms with water or juice for **drinking**." From **p. 5** "A benchmark for occasional single doses of psilocybin was around 1 g of dry Psilocybe cubensis but could vary between 0.25 g and as much as 3 g. An ideal dose for one individual could be far too much for another. The preferred dosage varied with the sensitivity of the user and the desired effects: 'You might have to experiment with the dose a bit because what works for one person does not necessarily work for another.' The potency of the material and particular type of

	mushrooms also called for different dosage: 'Around one gram of dried Cubensis is regularly used for a dose.' P. cubensis was the most common variety, but other species of mushrooms were also discussed: 'With Psilocybe azurescens or **Psilocybe cyanescens, 0.25 gram** should be sufficient.'" From **p. 6** "Those using the 'busting method' reported both acute and preventive treatment results, although it was described as crucial to follow a cyclic dosage scheme to obtain **long-term results**. Relapses were reported when the dosing regimen was not followed consistently: 'Mostly pain-free, except for when I did not take my proper preventative dose.' The busting method was reportedly effective with LSD, **psilocybin mushrooms**, and various kinds of LSA containing seeds." 2. BEUG (1982) "Psilocybin and psilocin levels in twenty species from seven genera of wild mushrooms in the Pacific Northwest, U.S.A." Journal of Ethnopharmacology. 5(3):271-285. From **p. 281**

TABLE 1

Psilocybin and psilocin levels in Pacific Northwest mushrooms as quantified by reversed phase HPLC

Species[1] (Figs. 1 - 20)	Date collected[2]	Psilocybin (mg/g dry weight)	Psilocin (mg/g dry weight)
Conocybe cyanopus (Atk.) Kühner	July 12, 1979	9.3	0
Conocybe tenera (Schaeff. ex Fr.) Kühner	Aug. 22, 1978	0	0
Conocybe sp. (near *lactea* (J. Lange) Métrod)	Aug. 13, 1978	0	0
Pholiotina filaris (Fr.) Singer	Oct. 1979	0	0
Panaeolus campanulatus (Fr.) Quél.	Aug. 13, 1978	0	0
	Sept. 4, 1978	0	0
	Mar. 18, 1980	0	0
Panaeolus acuminatus (Sec.) Quél.	Sept. 4, 1978	0	0
	Mar. 18, 1980	0	0
Panaeolus phalaenarum (Fr.) Quél.	July 23, 1978	0	0
	Cultivated	0	0
Psathyrella foenisecii (Fr.) Smith	June 18, 1978	0	0
	Oct. 4, 1978	0	0
Panaeolus semiovatus (Fr.) Lundell & Nanfeldt	June 28, 1978	0	0
	July 12, 1979 (3 collections)	0	0
Panaeolus subbalteatus (Berk. & Br.) Sacc.	July 3, 1978	3.5	0
	Sept. 5, 1978	6.5	0
	Sept. 3, 1979	1.6	0
Gymnopilus ventricosus (Earle) Hesler (generally identified as *G. spectabilis*)	Oct. 15, 1979	0	0
Stropharia aeruginosa (Fr.) Quél.	Oct. 29, 1979	0	0
Psilocybe semilanceata (Fr.) Quél.	Oct. 1979	6.9	0
	Sept. 4, 1978	10.8	0
	Oct. 22, 1979	12.0	0
	Nov. 5, 1979	6.9	0
	Nov. 27, 1979a	8.4	0
	Nov. 27, 1979b	12.8	0
	Nov. 27, 1979c	9.2	0
	Nov. 27, 1979d	6.6	0
	Nov. 27, 1979e	10.9	0
	Nov. 27, 1979f	8.5	0
Caps only	Nov. 27, 1979g	11.1	0
Stems only	Nov. 27, 1979g	6.2	0
Psilocybe cyanescens Wakefield	Oct. 1978a	4.9	1.7
	Oct. 28, 1979	1.5	9.6
	Nov. 2, 1979	8.2	1.3
	Nov. 6, 1979	11.5	7.6

TABLE 1 *(continued)*

Species[1] (Figs. 1 - 20)	Date collected[2]	Psilocybin (mg/g dry weight)	Psilocin (mg/g dry weight)
Psilocybe cyanescens	Nov. 7, 1979a	8.3	2.0
Wakefield	Nov. 7, 1979b	16.8	2.8
	Nov. 18, 1979a	14.3	2.8
	Nov. 18, 1979b	15.5	2.4
	Nov. 18, 1979c	13.6	2.3
	Nov. 18, 1979d	11.0	2.0
	Nov. 18, 1979e	10.1	1.4
	Nov. 18, 1979f	8.7	1.8
	Nov. 18, 1979g	9.7	2.8
	Nov. 19, 1979	8.4	0.6
Psilocybe stuntzii	Sept. 24, 1978	0	0
Guzmán & Ott	Oct. 27, 1979	3.6	0.6
	Oct. 31, 1979	0.4	0.12
	Nov. 13, 1979	3.6	0.06
Psilocybe baeocystis	Sept. 1979a	2.04	1.43
Singer & Smith	Sept. 1979b	1.96	1.32
	Sept. 1979c	1.92	0.48
	Sept. 1979d	2.04	3.07
	Sept. 5, 1979	8.5	5.9
	Oct. 1979a	2.8	0.8
	Oct. 1979b	1.5	0
Psilocybe coprophila (Bull. ex Fr.) Kummer	June 22, 1979	0	0
Psilocybe montana (Pers. ex Fr.) Kummer	Mar. 18, 1980	0	0
Psilocybe inquilina (Fr. ex Fr.) Bres.	Mar. 18, 1980	0	0
Psilocybe pelliculosa	Oct. 30, 1979	7.1	0
(Sm.) Singer & Smith	Oct. 8, 1979	4.1	0
	Nov. 8, 1979	1.2	0

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First Named Inventor/Applicant Name:	Emmanuelle SCHINDLER
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