IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Mind Medicine Inc	Confirmation No.: 2674
Serial No.:	18/196,992	Group No.: 2674
Filing or 371(c) Date:	12.05.2023	Examiner:

Entitled: DESOXYSCALINE DERIVATIVES WITH MODIDIED MESCALINE-LIKE ACTION

THIRD-PARTY PRE-ISSUANCE SUBMISSION

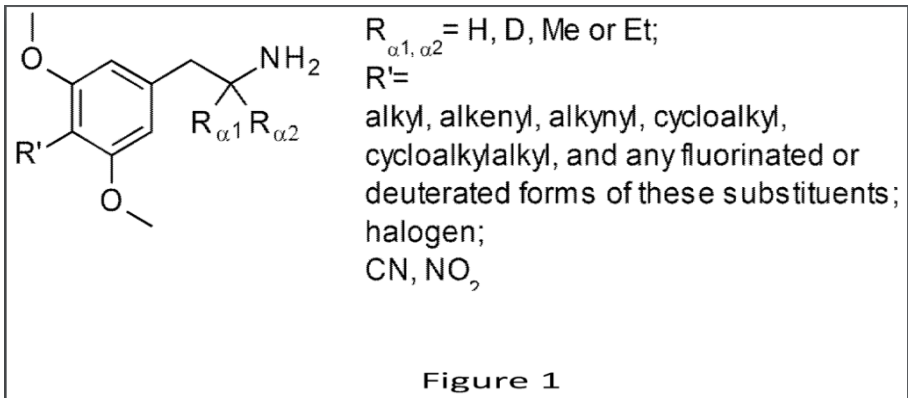
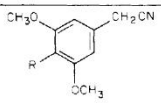
Examiner:

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.

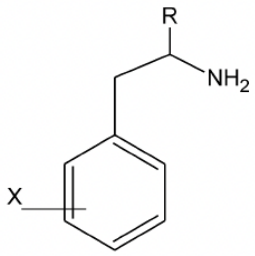
1. NICHOLS (1977) “Lipophilicity and Serotonin Agonist Activity in a Series of 4-Substitued Mescaline Derivatives” Journal of Medicinal Chemistry. Vol 20 (2): page 299-301.
2. THAKUR (2004) “QSAR Studies on Psychomimetic Phenylalkylamines” Bioorganic and Medicinal Chemistry. Vol 12: page 825-831.
3. DOWD (2000) “1-[4-(3-Phenylalkyl)phenyl]-2-aminopropanes as 5-HT_{2A} Partial Agonists” Journal of Medicinal Chemistry. Vol 43 (16): page 3074-3084.
4. PIKHAL (1996) “#18 4-BR-3,5-DMA” Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml
5. GUPTA (1983) “QSAR Studies on Hallucinogens” Chemical Reviews. Vol. 83: page 633-649.
6. BENINGTON (1960) “Mescaline Analogs” Journal of Organic Chemistry. Vol. 25 (11): 2066-2067.
7. WIKIDOC (2012) “Freebase (chemistry)”Wikidoc. Retrieved from August 9, 2012. URL: https://www.wikidoc.org/index.php/Freebase_(chemistry)
8. UTHAUG (2022) “The epidemiology of mescaline use: Pattern of use, motivations for consumption, and perceived consequences, benefits, and acute and enduring subjective effects” Journal of Psychopharmacology. Volume 0 (0): page 1-12.
9. Intl. Pub. No. WO2019079742A1 “Methods and systems for enhancing safety of psychedelic drug therapies” (Published 25 April 2019)

10. PIKHAL (1996) “#96 Mescaline” Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml

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.

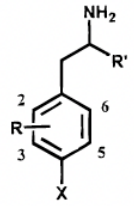
U.S.S.N. 18/196,992 Pending Claims	References
1. 1. A composition comprising a compound represented by FIG. 1, characterized in that R alpha1 and, independently and in any combination, R alpha2 is chosen from the group consisting of hydrogen, deuteron, methyl, ethyl, deuterated methyl (D 1-D 3), or deuterated ethyl (D 1-D 5), and further characterized in that R′ is one of the following substituents: C 1-C 5 branched or unbranched alkyl with the alkyl optionally substituted with F 1-F 11 fluorine and/or D 1-D 11 deuteron substituents up to a fully fluorinated and/or deuterated alkyl, C 3-C 6 cycloalkyl optionally and independently substituted with one or more substituents chosen from the group consisting of F 1-F 15 fluorine, D 1-D 15 deuteron, C 1-C 2 alkyl, and combinations thereof,	*Relevance of above figure to the application of interest, U.S. Application Number 18/196,992, as quoted from claim 1 of said application: “A composition comprising a compound represented by FIG. 1, characterized in that...*  Figure 1 • *Ra1 and Ra2 are...H or Me* • *R4 is Bromine or Me* 1. NICHOLS (1977) “Lipophilicity and Serotonin Agonist Activity in a Series of 4-Substitued Mescaline Derivatives” Journal of Medicinal Chemistry. Vol 20 (issue 2): page 299-301. Table I. 3,5-Dimethoxy-4-substituted Phenylacetonitriles  Compd no. | R | Mp or bp (mm), °C | Yield, % | Formula | Analyses 2a | OC_2H_5 | 57-58 | 86 | $C_{12}H_{13}NO_3$ | C, H, N 2b | O-*n*-C_3H_7 | 112-114 (0.1) | 75 | $C_{13}H_{17}NO_3$ | C, H, N 2c | O-*i*-C_3H_7 | 33-34 | 65 | $C_{13}H_{17}NO_3$ | C, H, N 2d | O-*n*-C_4H_9 | 42-43 | 87 | $C_{14}H_{19}NO_3$ | C, H, N 2e | $OCH_2C_6H_5$ | 66-67[a] | 84 | $C_{17}H_{17}NO_3$ | 2f | Br | 125-126 | 84[b] | $C_{10}H_{10}BrNO_3$ | C, H, N [a] Lit.[18] mp 64-65 °C. [b] Based on the chloride 6. 2. THAKUR (2004) “QSAR Studies on Psychomimetic Phenylalkylamines” Bioorganic and Medicinal Chemistry. Vol 12: page 825-831.

(C 3-C 6 cycloalkyl)-C 1-C 2 branched or unbranched alkyl optionally substituted with one or more substituents chosen from the group consisting of F 1-F 15 fluorine, D 1-D 15 deuteron, C 1-C 2 alkyl, and combinations thereof,
C 2-C 5 branched or unbranched alkenyl with E or Z or cis or trans double bond configuration, where any of the carbons of the branched or unbranched alkenyl substituent is substituted with a substituent chosen from the group consisting of C 1-C 2 alkyl, F 1-F 13 fluorine, D 1-D 13 deuteron, C 2 alkenyl, aryl or heteroaryl bearing zero up to any number of ether, thioether, halogen, alkyl, fluorinated alkyl, alkenyl, alkynyl or nitrogen-containing substituents, and combinations thereof,
C 2-C 5 branched or unbranched alkynyl where any of the carbons of the branched or unbranched alkynyl substituent is substituted with a substituent chosen from the group consisting of one or more C 1-C 2 alkyl, F 1-F 11 fluorine, D 1-D 11 deuteron, C 2 alkenyl, aryl or heteroaryl bearing zero up to any number of



Compd	X	R	LogMU (Obsd)
	2,5-OMe,4-I	Me	2.78
	2,5-OMe,4-Br	Me	2.72
	2,5-OMe,4-SEt	Me	1.96
	2,5-OMe,4-Et	Me	2.02
	2,5-OMe,4-Pr	Me	1.95
6	3,5-OMe,4-Br	Me	1.91

3. DOWD (2000) "1-[4-(3-Phenylalkyl)phenyl]-2-aminopropanes as 5-HT_{2A} Partial Agonists" Journal of Medicinal Chemistry. Vol 43 (issue 16): page 3074-3084.

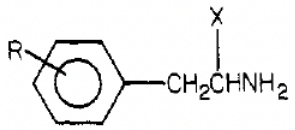


				receptor affinity; K_i, nM (SEM)	
	R	R′	X	5-HT_{2A}	5-HT_{2C}
1a	2,5-Di-OMe	-Me	Br	32 (4)	64 (12)
1b	2,5-Di-OMe	-H	-Br	16 (1)	190 (90)
19	2,5-Di-OMe	-Me	-H	4 720 (1,150)	>10 000
20	2,5-Di-OMe	-H	-H	3 000 (410)	5 520 (390)
21	2-OMe	-Me	-H	>10 000	>10 000
22	5-OMe[a]	-Me	-H	>10 000	>10 000
23	2,3-Di-OMe	-Me	-H	4 280 (460)	>10 000
24	3,5-Di-OMe	-Me	-H	>10 000	>10 000
25	3,5-Di-OMe	-Me	-Br	210 (45)	570 (110)
26	2,6-Di-OMe	-Me	-H	>10 000	>10 000
27	H	-Me	-H	>10 000	>10 000

4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml

#18 4-BR-3,5-DMA

3,5-DIMETHOXY-4-BROMOAMPHETAMINE

ether, thioether, halogen, alkyl, fluorinated alkyl, alkenyl, alkynyl or nitrogen-containing substituents, and combinations thereof, any halogen or a nitrogen-containing substituent of CN or NO 2.	5. GUPTA (1983) "QSAR Studies on Hallucinogens" Chemical Reviews. Vol. 83: page 633-649. 

compd	R	X	log RBR[a]	log P[a]
4	3,4,5-$(OCH_3)_3$	H	0.00	0.78
24	2,5-$(OCH_3)_2$-4-CH_3	CH_3	1.00	2.24
25	2,5-$(OCH_3)_2$-4-C_2H_5	CH_3	1.59	2.76
26	2,5-$(OCH_3)_2$-4-*n*-C_3H_7	CH_3	1.84	3.37
27	2,5-$(OCH_3)_2$-4-*n*-C_4H_9	CH_3	1.62	4.00
28	2,5-$(OCH_3)_2$-4-*n*-C_5H_{11}	CH_3	0.88	4.43
29	2,5-$(OCH_3)_2$-4-Br	CH_3	1.57	2.54
39	3,5-$(OCH_3)_2$-4-OC_2H_5	H	0.31	1.11
40	3,5-$(OCH_3)_2$-4-O-*n*-C_3H_7	H	0.56	1.70
53	2,5-$(OCH_3)_2$-4-SCH_3	CH_3	1.31	2.17
60	2,5-$(OCH_3)_2$-4-*t*-C_4H_9	CH_3	1.39	3.91
70	3,5-$(OCH_3)_2$-4-Br	H	0.88	2.03
71	3,5-$(OCH_3)_2$-4-*i*-C_3H_7	H	0.45	1.52
72	2,5-$(OCH_3)_2$-4-Br	H	0.83	1.81
73	3,5-$(OCH_3)_2$-4-O-*n*-C_4H_9	H	0.10	2.32
74	3,5-$(OCH_3)_2$-4-$OCH_2C_6H_5$	H	0.48	2.40
75	2,5-$(OCH_3)_2$-4-NO_2	CH_3	0.67	1.74

6. BENINGTON (1960) "Mescaline Analogs" Journal of Organic Chemistry. Vol. 25 (11): 2066-2067.

3,5-Dimethoxy-4-methyl-β-phenethylamine. To a stirred solution of 6.8 g. of lithium aluminum hydride in 200 ml. of dry absolute ether was added a slurry of 10 g. of 3,5-dimethoxy-4-methylphenylacetamide in 125 ml. of hot dry reagent benzene, using part of the benzene to rinse in the last of the amide. The resulting mixture was stirred and refluxed for 1 hr., cooled in an ice bath, and hydrolyzed by slow and cautious addition of water. The ether solution of the amine obtained after filtration from inorganic matter and drying (anhydrous magnesium sulfate) was treated with dry hydrogen chloride to precipitate the product as its hydrochloride salt; yield, 8.9 g. (80%); m.p. 233–235°. Recrystallization from ethanol–ethyl acetate raised the melting point to 244–245°.

Anal. Calcd. for $C_{11}H_{18}ClNO_2$: C, 57.0; H, 7.8; Cl, 15.3. Found: C, 56.2; H, 8.0; Cl, 15.2.

2. The composition of claim 1, wherein said compound is a free base	7. WIKIDOC (2012) "Freebase (chemistry)"Wikidoc. Retrieved from August 9, 2012. URL: https://www.wikidoc.org/index.php/Freebase_(chemistry)

	From **Paragraph 1**: Freebase refers to the standalone basic form of an amine, usually an alkaloid natural product, as opposed to its water-soluble salt form. Most alkaloids are unstable and corrosive in their freebase form, and thus are usually stored in salt form. The salt form is the neutral amine compound with an additional proton, which is positively charged, plus a negative counterion. **Freebase amines are often found as hydrochloride salt, although other negative counterions are found, such as acetate, oxalate, bromide, et cetera.**
3. The composition of claim 1, wherein said compound is a salt thereof.	3. DOWD (2000) "1-[4-(3-Phenylalkyl)phenyl]-2-aminopropanes as 5-HT2A Partial Agonists" Journal of Medicinal Chemistry. Vol 43 (issue 16): page 3074-3084. From **Synthesis**: **1-(4-Bromo-3,5-dimethoxyphenyl)-2-aminopropane HCl (25)** 4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Synthesis**: The starting material 3,5-dimethoxy-4-bromobenzoic acid (made from the commercially available resorcinol by the action of methyl sulfate) was a white crystalline solid from aqueous EtOH with a mp of 248-250 °C. Reaction with thionyl chloride produced 3,5-dimethoxy-4-bromobenzoyl chloride which was used as the crude solid product, mp 124-128 °C. This was reduced with tri-O-(t)-butoxy lithium aluminum hydride to produce 3,5-dimethoxy-4-bromobenzaldehyde which was recrystallized from aqueous MeOH and had a mp of 112-114 °C. Anal. (C9H9BrO3) C,H. This aldehyde, with nitroethane and anhydrous ammonium acetate in acetic acid, was converted to the nitrostyrene 1-(3,5-dimethoxy-4-bromophenyl)-2-nitropropene, with a mp of 121-121.5 °C. Anal. (C11H12BrNO4) C,H,N. This was reduced at low temperature with just one equivalent of LAH, to minimize reductive removal of the bromine atom. **The product 3,5-dimethoxy-4-bromoamphetamine hydrochloride** (4-BR-3,5-DMA) was isolated in a 37% yield and had a mp of 221-222 °C. Anal. (C11H17BrClNO2) C,H,N.
4. The composition of claim 3, wherein said compound is a hydrochloride salt thereof	3. DOWD (2000) "1-[4-(3-Phenylalkyl)phenyl]-2-aminopropanes as 5-HT2A Partial Agonists" Journal of Medicinal Chemistry. Vol 43 (issue 16): page 3074-3084. From **Synthesis**: **1-(4-Bromo-3,5-dimethoxyphernyl)-2-aminopropane HCl (25)**...

	4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Synthesis**: The starting material 3,5-dimethoxy-4-bromobenzoic acid (made from the commercially available resorcinol by the action of methyl sulfate) was a white crystalline solid from aqueous EtOH with a mp of 248-250 °C. Reaction with thionyl chloride produced 3,5-dimethoxy-4-bromobenzoyl chloride which was used as the crude solid product, mp 124-128 °C. This was reduced with tri-O-(t)-butoxy lithium aluminum hydride to produce 3,5-dimethoxy-4-bromobenzaldehyde which was recrystallized from aqueous MeOH and had a mp of 112-114 °C. Anal. (C9H9BrO3) C,H. This aldehyde, with nitroethane and anhydrous ammonium acetate in acetic acid, was converted to the nitrostyrene 1-(3,5-dimethoxy-4-bromophenyl)-2-nitropropene, with a mp of 121-121.5 °C. Anal. (C11H12BrNO4) C,H,N. This was reduced at low temperature with just one equivalent of LAH, to minimize reductive removal of the bromine atom. **The product 3,5-dimethoxy-4-bromoamphetamine hydrochloride** (4-BR-3,5-DMA) was isolated in a 37% yield and had a mp of 221-222 °C. Anal. (C11H17BrClNO2) C,H,N. 6. BENINGTON (1960) "Mescaline Analogs" Journal of Organic Chemistry. Vol 25 (11): 2066-2067. *3,5-Dimethoxy-4-methyl-β-phenethylamine.* To a stirred solution of 6.8 g. of lithium aluminum hydride in 200 ml. of dry absolute ether was added a slurry of 10 g. of 3,5-dimethoxy-4-methylphenylacetamide in 125 ml. of hot dry reagent benzene, using part of the benzene to rinse in the last of the amide. The resulting mixture was stirred and refluxed for 1 hr., cooled in an ice bath, and hydrolyzed by slow and cautious addition of water. The ether solution of the amine obtained after filtration from inorganic matter and drying (anhydrous magnesium sulfate) was treated with dry hydrogen chloride to precipitate the product as its hydrochloride salt; yield, 8.9 g. (80%); m.p. 233–235°. Recrystallization from ethanol–ethyl acetate raised the melting point to 244–245°. *Anal.* Calcd. for $C_{11}H_{18}ClNO_2$: C, 57.0; H, 7.8; Cl, 15.3. Found: C, 56.2; H, 8.0; Cl, 15.2.
5. The composition of claim 4, wherein said compound is a pharmacologically acceptable acid addition salt thereof chosen	3. DOWD (2000) "1-[4-(3-Phenylalkyl)phenyl]-2- aminopropanes as 5-HT2A Partial Agonists" Journal of Medicinal Chemistry. Vol 43 (issue 16): page 3074-3084.

from the group consisting of sulfate, pyrosulfate, bisulfate, sulfite, bisulfite, phosphate, monohydrogen-phosphate, dihydrogenphosphate, metaphosphate, pyro-phosphate, chloride, bromide, iodide, formate, acetate, propionate, decanoate, caprylate, acrylate, isobutyrate, caproate, heptanoate, oxalate, malonate, succinate, suberate, sebacate, fumarate, maleate, benzoate, phthalate, sulfonate, phenylacetate, citrate, lactate, glycollate, tartrate, methanesulfonate, propanesulfonate, and mandelate.	From **Synthesis**: **1-(4-Bromo-3,5-dimethoxyphernyl)-2-aminopropane HCl (25)**... 4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Synthesis**: The starting material 3,5-dimethoxy-4-bromobenzoic acid (made from the commercially available resorcinol by the action of methyl sulfate) was a white crystalline solid from aqueous EtOH with a mp of 248-250 °C. Reaction with thionyl chloride produced 3,5-dimethoxy-4-bromobenzoyl chloride which was used as the crude solid product, mp 124-128 °C. This was reduced with tri-O-(t)-butoxy lithium aluminum hydride to produce 3,5-dimethoxy-4-bromobenzaldehyde which was recrystallized from aqueous MeOH and had a mp of 112-114 °C. Anal. (C9H9BrO3) C,H. This aldehyde, with nitroethane and anhydrous ammonium acetate in acetic acid, was converted to the nitrostyrene 1-(3,5-dimethoxy-4-bromophenyl)-2-nitropropene, with a mp of 121-121.5 °C. Anal. (C11H12BrNO4) C,H,N. This was reduced at low temperature with just one equivalent of LAH, to minimize reductive removal of the bromine atom. **The product 3,5-dimethoxy-4-bromoamphetamine hydrochloride** (4-BR-3,5-DMA) was isolated in a 37% yield and had a mp of 221-222 °C. Anal. (C11H17BrClNO2) C,H,N.
6. The composition of claim 1, wherein said compound is chosen from the group consisting of a racemate, a single enantiomer, a diastereomer, and a mixture of enantiomers or diastereomers in any ratio, a single and a mixture E or Z configurational isomer in any ratio, a single and a mixture cis or trans configurational isomer in any ratio, and any combination thereof.	4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Synthesis**: The starting material 3,5-dimethoxy-4-bromobenzoic acid (made from the commercially available resorcinol by the action of methyl sulfate) was a white crystalline solid from aqueous EtOH with a mp of 248-250 °C. Reaction with thionyl chloride produced 3,5-dimethoxy-4-bromobenzoyl chloride which was used as the crude solid product, mp 124-128 °C. This was reduced with tri-O-(t)-butoxy lithium aluminum hydride to produce 3,5-dimethoxy-4-bromobenzaldehyde which was recrystallized from aqueous MeOH and had a mp of 112-114 °C. Anal. (C9H9BrO3) C,H. This aldehyde, with nitroethane and anhydrous ammonium acetate in acetic acid, was converted to the nitrostyrene 1-(3,5-dimethoxy-4-bromophenyl)-2-nitropropene, with a mp of 121-121.5 °C. Anal. (C11H12BrNO4) C,H,N. This was reduced at low temperature with just one equivalent of LAH, to minimize reductive removal of the bromine atom. **The product 3,5-dimethoxy-4-bromoamphetamine hydrochloride** (4-BR-3,5-DMA) was

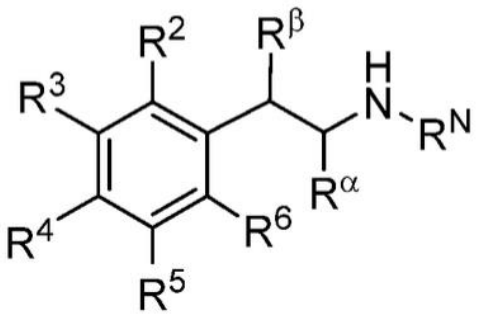
	isolated in a 37% yield and had a mp of 221-222 °C. Anal. (C11H17BrClNO2) C,H,N.
7. A method of changing neurotransmission, including the steps of: administering a pharmaceutically effective amount of composition to a mammal of a compound represented by FIG. 1, which is characterized in that R alpha1 and, independently and in any combination, R alpha2 is chosen from the group consisting of hydrogen, deuteron, methyl, ethyl, deuterated methyl (D 1-D 3), or deuterated ethyl (D 1-D 5), and further characterized in that R′ is one of the following substituents: C 1-C 5 branched or unbranched alkyl with the alkyl optionally substituted with F 1-F 11 fluorine and/or D 1-D 11 deuteron substituents up to a fully fluorinated and/or deuterated alkyl, C 3-C 6 cycloalkyl optionally and independently substituted with one or more substituents chosen from the group consisting of F 1-F 15 fluorine, D 1-D 15 deuteron, C 1-C 2 alkyl, and combinations thereof, (C 3-C 6 cycloalkyl)-C 1-C 2 branched or	4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Qualitative Comments**: (with 3 mg) **This is certainly no placebo**. At about 2 hours I felt some **analgesia and numbing** in my extremities, but if there were any sensory distortions, they were barely perceptible. (with 6 mg) There is a very shallow threshold, no more. (with 10 mg) **I can certainly confirm the indications of anesthesia that were hinted at. It was for me central in nature, however**. I could (this at three hours) pierce a skin pinch on my left arm with no bother except for the emerging of the needle due to skin resistance. There was little bleeding. And multiple needle prickings into the thumb abductor were not felt. A quick plunge of the tip of my little finger into boiling water elicited reflex response, but no residual pain. **Judgment was OK, so I stayed out of physical trouble, luckily! The perhaps ++ was dropping in the fourth or fifth hour, and by the tenth hour there were few effects still noted, except for some teeth-rubbiness and a burning irritation at the pin-prick area, so feeling is back.** No sleep problems at just past midnight.

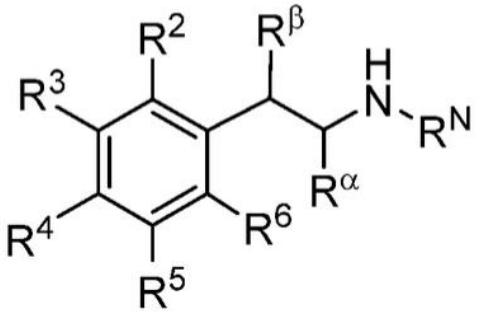
unbranched alkyl optionally substituted with one or more substituents chosen from the group consisting of F 1-F 15 fluorine, D 1-D 15 deuteron, C 1-C 2 alkyl, and combinations thereof, C 2-C 5 branched or unbranched alkenyl with E or Z or cis or trans double bond configuration, where any of the carbons of the branched or unbranched alkenyl substituent is substituted with a substituent chosen from the group consisting of C 1-C 2 alkyl, F 1-F 13 fluorine, D 1-D 13 deuteron, C 2 alkenyl, aryl or heteroaryl bearing zero up to any number of ether, thioether, halogen, alkyl, fluorinated alkyl, alkenyl, alkynyl or nitrogen-containing substituents, and combinations thereof, C 2-C 5 branched or unbranched alkynyl where any of the carbons of the branched or unbranched alkynyl substituent is substituted with a substituent chosen from the group consisting of one or more C 1-C 2 alkyl, F 1-F 11 fluorine, D 1-D 11 deuteron, C 2 alkenyl, aryl or heteroaryl bearing zero up to any number of ether, thioether, halogen, alkyl,	

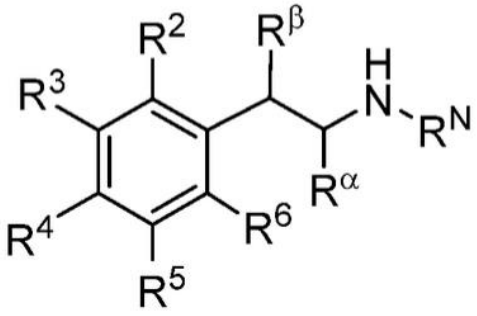
fluorinated alkyl, alkenyl, alkynyl or nitrogen-containing substituents, and combinations thereof, any halogen or a nitrogen-containing substituent of CN or NO 2; increasing serotonin 5-HT2A and 5-HT2C receptor interaction in the mammal; and inducing psychoactive effects.	
8. The method of claim 7, wherein the compound is chosen from the group consisting of a racemate, a single enantiomer, a diastereomer, a mixture of enantiomers or diastereomers in any ratio, a single and a mixture E or Z configurational isomer in any ratio, a single and a mixture cis or trans configurational isomer in any ratio, and any combination thereof.	4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Synthesis**: The starting material 3,5-dimethoxy-4-bromobenzoic acid (made from the commercially available resorcinol by the action of methyl sulfate) was a white crystalline solid from aqueous EtOH with a mp of 248-250 °C. Reaction with thionyl chloride produced 3,5-dimethoxy-4-bromobenzoyl chloride which was used as the crude solid product, mp 124-128 °C. This was reduced with tri-O-(t)-butoxy lithium aluminum hydride to produce 3,5-dimethoxy-4-bromobenzaldehyde which was recrystallized from aqueous MeOH and had a mp of 112-114 °C. Anal. (C9H9BrO3) C,H. This aldehyde, with nitroethane and anhydrous ammonium acetate in acetic acid, was converted to the nitrostyrene 1-(3,5-dimethoxy-4-bromophenyl)-2-nitropropene, with a mp of 121-121.5 °C. Anal. (C11H12BrNO4) C,H,N. This was reduced at low temperature with just one equivalent of LAH, to minimize reductive removal of the bromine atom. **The product 3,5-dimethoxy-4-bromoamphetamine hydrochloride** (4-BR-3,5-DMA) was isolated in a 37% yield and had a mp of 221-222 °C. Anal. (C11H17BrClNO2) C,H,N. From **Qualitative Comments**: (with 3 mg) **This is certainly no placebo**. At about 2 hours I felt some **analgesia and numbing** in my extremities, but if there were any sensory distortions, they were barely perceptible. (with 6 mg) There is a very shallow threshold, no more. (with 10 mg) **I can certainly confirm the indications of anesthesia that were hinted at. It was for me central in nature, however**. I could (this at three hours) pierce a skin pinch on my left arm with no bother except for the emerging of the needle due to skin resistance. There was little bleeding. And multiple needle prickings into the thumb abductor were not felt. A quick

	plunge of the tip of my little finger into boiling water elicited reflex response, but no residual pain. **Judgment was OK, so I stayed out of physical trouble, luckily! The perhaps ++ was dropping in the fourth or fifth hour, and by the tenth hour there were few effects still noted, except for some teeth-rubbiness and a burning irritation at the pin-prick area, so feeling is back.** No sleep problems at just past midnight.
8. The method of claim 7, wherein the compound is chosen from the group consisting of a racemate, a single enantiomer, a diastereomer, a mixture of enantiomers or diastereomers in any ratio, a single and a mixture E or Z configurational isomer in any ratio, a single and a mixture cis or trans configurational isomer in any ratio, and any combination thereof.	4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Synthesis**: The starting material 3,5-dimethoxy-4-bromobenzoic acid (made from the commercially available resorcinol by the action of methyl sulfate) was a white crystalline solid from aqueous EtOH with a mp of 248-250 °C. Reaction with thionyl chloride produced 3,5-dimethoxy-4-bromobenzoyl chloride which was used as the crude solid product, mp 124-128 °C. This was reduced with tri-O-(t)-butoxy lithium aluminum hydride to produce 3,5-dimethoxy-4-bromobenzaldehyde which was recrystallized from aqueous MeOH and had a mp of 112-114 °C. Anal. (C9H9BrO3) C,H. This aldehyde, with nitroethane and anhydrous ammonium acetate in acetic acid, was converted to the nitrostyrene 1-(3,5-dimethoxy-4-bromophenyl)-2-nitropropene, with a mp of 121-121.5 °C. Anal. (C11H12BrNO4) C,H,N. This was reduced at low temperature with just one equivalent of LAH, to minimize reductive removal of the bromine atom. **The product 3,5-dimethoxy-4-bromoamphetamine hydrochloride** (4-BR-3,5-DMA) was isolated in a 37% yield and had a mp of 221-222 °C. Anal. (C11H17BrClNO2) C,H,N. From **Qualitative Comments**: (with 3 mg) **This is certainly no placebo**. At about 2 hours I felt some **analgesia and numbing** in my extremities, but if there were any sensory distortions, they were barely perceptible. (with 6 mg) There is a very shallow threshold, no more. (with 10 mg) **I can certainly confirm the indications of anesthesia that were hinted at. It was for me central in nature, however**. I could (this at three hours) pierce a skin pinch on my left arm with no bother except for the emerging of the needle due to skin resistance. There was little bleeding. And multiple needle prickings into the thumb abductor were not felt. A quick plunge of the tip of my little finger into boiling water elicited reflex response, but no residual pain. **Judgment was OK, so I stayed out of physical trouble, luckily! The perhaps ++ was dropping in the fourth or fifth hour, and by the tenth hour there were few effects still noted, except for some teeth-rubbiness and a burning irritation at the pin-prick area, so feeling is back.** No sleep problems at just past midnight.

9. The method of claim 7, wherein the psychoactive effects include psychedelic or empathogenic effects having intensity, effect quality, or duration of effect in a mammal in comparison to that of mescaline.	4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Duration**: **8-12 hours** 8. UTHAUG (2022) "The epidemiology of mescaline use: Pattern of use, motivations for consumption, and perceived consequences, benefits, and acute and enduring subjective effects" Journal of Psychopharmacology. Volume 0 (0): page 1-12. From **Introduction**: Oral ingestion of mescaline appears to have a longer half-life compared to other classic psychedelics (i.e. 6 h), with peak effects occurring approximately 2 h after ingestion and a **total duration lasting 8–12 h**
10. The method of claim 7, wherein the compound is administered to mammals for substance-assisted psychotherapy.	9. Intl. Pub. No. WO2019079742A1 "Methods and systems for enhancing safety of psychedelic drug therapies" (Published 25 April 2019) From claim 21 "A **method of providing a regimen of psychedelic therapy to a patient**..." From claim 184 "The **method of any one of claims 1 -183**, wherein the psychedelic therapy is part of a complex therapy, **wherein the patient is additionally being treated with a psychotherapy**" From claim 194 "The **method of any one of claims 1 -193**, **wherein the psychedelic therapy comprises administration of an agent** selected from the group consisting **of a 5-HT2A receptor agonist**, an empathogenic agent, and a dissociative agent." From claim 195 "The **method of claim 194**, **wherein the psychedelic therapy comprises administration of a 5- HT2A receptor agonist**." From claim 196 "The method of claim 195, **wherein the 5-HT2A receptor agonist is...formula (II)**..." From page 15 "...a compound of **formula (II),** wherein **Ralpha, Rbeta, R2, R3, R4, R5, R6, and/or RN are selected from** the group consisting of **OCH3,** CH3, SCH3, **Br, I,** CH2CH(CH3)2, and **H**" From page 15 "formula (II):

	
11. The method of claim 7, wherein the compound is administered to allow for changing dose potency in comparison to mescaline.	4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Dosage**: **4-10 mg** 8. UTHAUG (2022) "The epidemiology of mescaline use: Pattern of use, motivations for consumption, and perceived consequences, benefits, and acute and enduring subjective effects" Journal of Psychopharmacology. Volume 0 (0): page 1-12. From **Introduction**: **Effective oral dosage of synthetic mescaline is in the 200–400 mg range**...
12. The method of claim 7, wherein the compound is administered to allow for tailoring and treatment individualization to the mammal's therapeutic need.	9. Intl. Pub. No. WO2019079742A1 "Methods and systems for enhancing safety of psychedelic drug therapies" (Published 25 April 2019) From claim 21 "A **method of providing a regimen of psychedelic therapy to a patient**, the method comprising**:** (i) **providing a differential measure of risk obtained by comparing two or more measures of risk,** each measure of risk derived from one or more language characteristics of a language sample obtained from the patient, wherein the one or more measures of risk correlates with the risk of precipitating or exacerbating psychosis, hypomania, or mania in the patient, and wherein each measure of risk is associated with a different treatment time point; and (ii) **suspending the psychedelic therapy if the differential measure of risk exceeds a predetermined threshold**." From claim 184 "The **method of any one of claims 1 -183**, wherein the psychedelic therapy is part of a complex therapy, **wherein the patient is additionally being treated with a psychotherapy**" From claim 194 "The **method of any one of claims 1 -193**, **wherein the psychedelic therapy comprises administration of an agent** selected from

	the group consisting **of a 5-HT2A receptor agonist**, an empathogenic agent, and a dissociative agent." From claim 195 "The **method of claim 194**, **wherein the psychedelic therapy comprises administration of a 5- HT2A receptor agonist**." From claim 196 "The method of claim 195, **wherein the 5-HT2A receptor agonist is...formula (II)**..." From page 15 "...a compound of **formula (II),** wherein **Ralpha, Rbeta, R2, R3, R4, R5, R6, and/or RN are selected from** the group consisting of **OCH3,** CH3, SCH3, **Br, I,** CH2CH(CH3)2, and **H**" From page 15 "formula (II): 
13. The method of claim 10, wherein the mammal is a human.	9. Intl. Pub. No. WO2019079742A1 "Methods and systems for enhancing safety of psychedelic drug therapies" (Published 25 April 2019) From claim 21 "A **method of providing a regimen of psychedelic therapy to a patient**..." From claim 184 "The **method of any one of claims 1 -183**, wherein the psychedelic therapy is part of a complex therapy, **wherein the patient is additionally being treated with a psychotherapy**" From claim 194 "The **method of any one of claims 1 -193**, **wherein the psychedelic therapy comprises administration of an agent** selected from the group consisting **of a 5-HT2A receptor agonist**, an empathogenic agent, and a dissociative agent." From claim 195 "The **method of claim 194**, **wherein the psychedelic therapy comprises administration of a 5- HT2A receptor agonist**." From claim 196 "The method of claim 195, **wherein the 5-HT2A receptor agonist is...formula (II)**..."

	From page 15 "...a compound of **formula (II),** wherein **Ralpha, Rbeta, R2, R3, R4, R5, R6, and/or RN are selected from** the group consisting of **OCH3,** CH3, SCH3, **Br, I,** CH2CH(CH3)2, and **H**" From page 15 "formula (II): 
17. The method of claim 16, wherein the positive effects are chosen from the group consisting of more overall positive effects, more or less perceptual effects, more emotional effects, and combinations thereof.	4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Duration**: **8-12 hours** 10. PIKHAL (1996) "#96 Mescaline" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Duration**: **10-12 hours**
18. The method of claim 14, further including the step of providing a shorter duration of action of the desoxyscaline derivative than with other psychedelics.	4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Duration**: **8-12 hours** 10. PIKHAL (1996) "#96 Mescaline" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Duration**: **10-12 hours**
20. A method of changing neurotransmission of an individual, including the steps of:	4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Qualitative Comments**: (with 3 mg) **This is certainly no placebo**. At about 2 hours I felt some analgesia and numbing in my extremities, but if there were any sensory distortions, they were barely perceptible.

administering a desoxyscaline derivative; and changing neurotransmission in the individual.	(with 6 mg) There is a very shallow threshold, no more. (with 10 mg) **I can certainly confirm the indications of anesthesia that were hinted at. It was for me central in nature, however**. I could (this at three hours) pierce a skin pinch on my left arm with no bother except for the emerging of the needle due to skin resistance. There was little bleeding. And multiple needle prickings into the thumb abductor were not felt. A quick plunge of the tip of my little finger into boiling water elicited reflex response, but no residual pain. **Judgment was OK, so I stayed out of physical trouble, luckily! The perhaps ++ was dropping in the fourth or fifth hour, and by the tenth hour there were few effects still noted, except for some teeth-rubbiness and a burning irritation at the pin-prick area, so feeling is back.** No sleep problems at just past midnight.
21. The method of claim 20, wherein the desoxyscaline derivative is further defined as a compound represented by FIG. 1, which is characterized in that R alpha1 and, independently and in any combination, R alpha2 is chosen from the group consisting of hydrogen, deuteron, methyl, ethyl, deuterated methyl (D 1-D 3), or deuterated ethyl (D 1-D 5), and further characterized in that R′ is one of the following substituents: C 1-C 5 branched or unbranched alkyl with the alkyl optionally substituted with F 1-F 11 fluorine and/or D 1-D 11 deuteron substituents up to a fully fluorinated and/or deuterated alkyl, C 3-C 6 cycloalkyl optionally and independently substituted with one or more substituents	4. PIKHAL (1996) "#18 4-BR-3,5-DMA" Erowid. Retrieved from March 8, 2000. URL: https://www.erowid.org/library/books_online/pihkal/pihkal018.shtml From **Qualitative Comments**: (with 3 mg) **This is certainly no placebo**. At about 2 hours I felt some analgesia and numbing in my extremities, but if there were any sensory distortions, they were barely perceptible. (with 6 mg) There is a very shallow threshold, no more. (with 10 mg) **I can certainly confirm the indications of anesthesia that were hinted at. It was for me central in nature, however**. I could (this at three hours) pierce a skin pinch on my left arm with no bother except for the emerging of the needle due to skin resistance. There was little bleeding. And multiple needle prickings into the thumb abductor were not felt. A quick plunge of the tip of my little finger into boiling water elicited reflex response, but no residual pain. **Judgment was OK, so I stayed out of physical trouble, luckily! The perhaps ++ was dropping in the fourth or fifth hour, and by the tenth hour there were few effects still noted, except for some teeth-rubbiness and a burning irritation at the pin-prick area, so feeling is back.** No sleep problems at just past midnight.

chosen from the group consisting of F 1-F 15 fluorine, D 1-D 15 deuteron, C 1-C 2 alkyl, and combinations thereof, (C 3-C 6 cycloalkyl)-C 1-C 2 branched or unbranched alkyl optionally substituted with one or more substituents chosen from the group consisting of F 1-F 15 fluorine, D 1-D 15 deuteron, C 1-C 2 alkyl, and combinations thereof, C 2-C 5 branched or unbranched alkenyl with E or Z or cis or trans double bond configuration, where any of the carbons of the branched or unbranched alkenyl substituent is substituted with a substituent chosen from the group consisting of C 1-C 2 alkyl, F 1-F 13 fluorine, D 1-D 13 deuteron, C 2 alkenyl, aryl or heteroaryl bearing zero up to any number of ether, thioether, halogen, alkyl, fluorinated alkyl, alkenyl, alkynyl or nitrogen-containing substituents, and combinations thereof, C 2-C 5 branched or unbranched alkynyl where any of the carbons of the branched or unbranched alkynyl substituent is substituted with a substituent chosen from the group consisting of	

one or more C 1-C 2 alkyl, F 1-F 11 fluorine, D 1-D 11 deuteron, C 2 alkenyl, aryl or heteroaryl bearing zero up to any number of ether, thioether, halogen, alkyl, fluorinated alkyl, alkenyl, alkynyl or nitrogen-containing substituents, and combinations thereof, any halogen or, a nitrogen-containing substituent of CN or NO 2.	

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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/196,992	**03/07/2024 10:40:41 AM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Jeremy Rolquin
PATENT CENTER #	64585060	FILING DATE	05/12/2023
CUSTOMER #	–	FIRST NAMED INVENTOR	
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	-

Documents

TOTAL DOCUMENTS: 23

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
Concise-description-generated.pdf		2	Concise Description of Relevance	37 KB
third-party-preissuance-submission.pdf		3	Third-Party Submission Under 37 CFR 1.290	75 KB
Third-party-notification-request.pdf		1	Request for Notification of Non-compliant Third-Party Submission	13 KB
4_PIKHAL.pdf		534	-	2442 KB
4_PIKHAL-NPL.pdf	(1-534)	534	Non Patent Literature	2425 KB
4_PIKHAL-NPL.pdf	(1-534)	534	Non Patent Literature	2425 KB
Mind Med 3PS Final_Embedded.pdf		18	-	1004 KB
Mind Med 3PS	(1-18)	18	Concise Description of	1005 KB

Final_Embedded- 3P.RELEVANCE.pdf			Relevance	
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8_Uthaug.pdf	E76151B7BF88580677B4FDADCD16C81AE6947AC4E45551C4578115781ED2792254627698F04BFFE2763B33B4AD8CA5109CD31768F7DBC7A8DEEB7091FBBDD52C
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9_WO2019079742A1-FOR.pdf	04A9AA11312BE0D17A3802C7616E025D369F39E5A14BF5EF59D2ECA9672AFC7A4BDB0B462A6E558A4256547A8D984CDE6A7785280FCB923C9FAC985F8A6BD796
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6_Benington_Embedded.pdf	90E10E7832266AE80E155349A768B33452805481400F13859FCB6D9D3031002F561E2731BBFAFE96EE64BBD680CAEAB8FFF89B571C9FA7D7FA891AB0B38FD6C0
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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

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If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/196,992	**03/07/2024 10:40:41 AM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Jeremy Rolquin
PATENT CENTER #	64585060	AUTHORIZED BY	-
CUSTOMER #	–	FILING DATE	05/12/2023
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
CARD / 9499	**E202437A41247200**	**Jeremy Rolquin**

FEE CODE	DESCRIPTION	ITEM PRICE($)	QUANTITY	ITEM TOTAL($)
2818	DOCUMENT FEE FOR THIRD-PARTY SUBMISSIONS (SEE 37 CFR 1.290(F))	72.00	1	72.00
			TOTAL AMOUNT:	**$72.00**

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

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