IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	MiHKAL GmbH	Confirmation No.: 6509
Serial No.:	18/024,517	Group No.:
Filing or 371(c) Date:	03 March 2023	Examiner:

Entitled: NOVEL SAFRYLAMINE DERIVATIVES HAVING PRODRUG PROPERTIES

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. US Priority Doc. No. 63/115,245 of US Pat. Doc. No. 17/518,846 “MDMA PRODRUGS TO ASSIST PSYCHOTHERAPY” (Priority doc filed 18 November 2020).

2. U.S. Pat. App. Doc. No. 2009/0131335 “ABUSE-RESISTANT AMPHETAMINE PRODRUGS” (Published 21 May 2009).

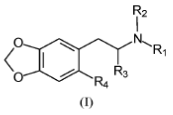
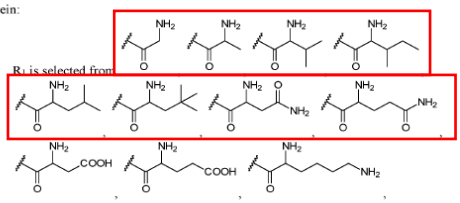
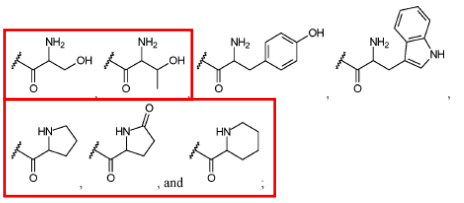
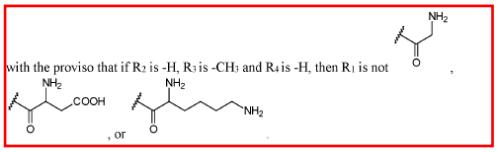
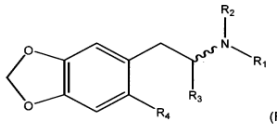
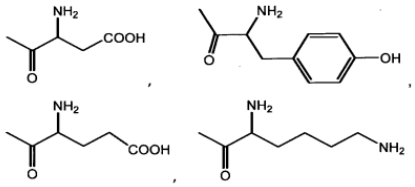
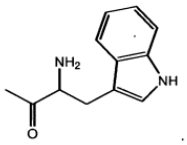
3. MAZUR (1970) “Structure-taste relation of aspartic acid amides” J. Med. Chem. Vol 13(6): 1217-1221.

4. Gatch (2016) “Locomotor, discriminative stimulus, and place conditioning effects of MDAI in rodents” Behavioral Pharmacology, Vol. 27 (6): 497-505.

5. Nichols (1986) “Synthesis and Evaluation of 2,3-Dihydrobenzofuran Analogues of the Hallucinogen 1-(2,5-Dimethoxy-4methylphenyl)-2-aminopropane: Drug Discrimination Studies in Rats” Journal of Medicinal Chemistry, Vol. 29 (2): 302-304.

6. Bahji (2019) “Efficacy of 3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy for posttraumatic stress disorder: A systematic review and meta-analysis” Progress in Neuropsychopharmacology & Biological Psychiatry, Vol. 96, 109735.

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.#18/024,517 Pending Claims	References
1. A compound according to the general formula (I):  (I) wherein:  R1 is selected from  , and ; R2 is -H or -CH3; and R3 is -CH3, and R4 is -H or -OCH3, or R3 and R4 are mutually joined to form a group -CH2-; or a pharmaceutically acceptable salt thereof;  with the proviso that if R2 is -H, R3 is -CH3 and R4 is -H, then R1 is not , or	*From the application of interest's priority document DE 10 2020 123 793.6 (filed 11 September 2020):* From **claim 1**: "1. 3,4-methylenedioxy-amphetamine peptide according to general formula I:  (Formel I) where R1 is selected from the group consisting of:  und  where R2 is selected from the group consisting of: -H or -CH3. where R3 is selected from the group consisting of: -CH3 or -CH2-R4 where R4 is selected from the group consisting of: -H, -OCH3, or R3-CH2-" 1. US Priority Doc. No. 63/115,245 of US Pat. Doc. No. 17/518,846 "MDMA PRODRUGS TO ASSIST PSYCHOTHERAPY" (Priority doc filed 18 November 2020). From **claim 1**: "A compound comprising a prodrug including a psychoactive base substance attached to an amino acid." From **claim 3**: "The compound of claim 2, wherein the MDMA or MDMA-like substance is chosen from the group consisting of MDA…MDAI…mixed dopaminergic-serotonergic amphetamine and their N-alkylated analogs..." From **claim 4**: "The compound of claim 1, wherein said amino acid is chosen from the group consisting of lysine, alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine,

leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine."

From **claim 5**: "The compound of claim 1, wherein the amino acid is chosen from the group consisting of natural or synthetic."

Figure 1A:

Fig. 1A

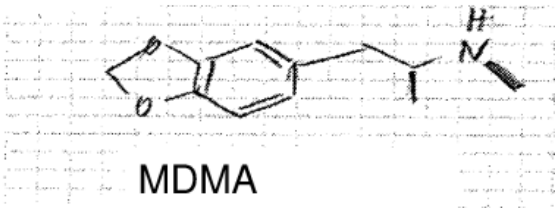
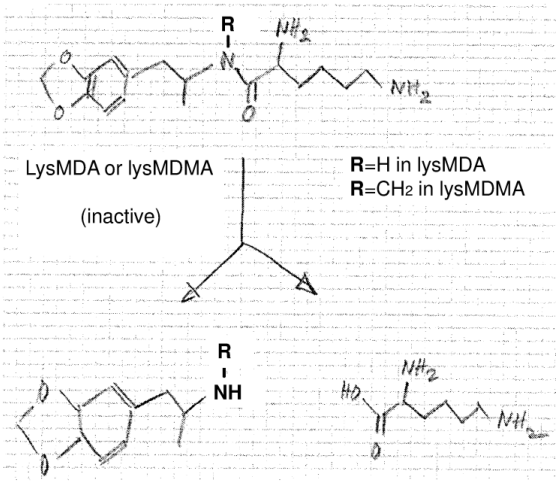


Figure 2:

Fig. 2



2. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009).

From **claim 1**: "A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt thereof, said method comprising orally administering to said subject a prodrug or a salt thereof said **prodrug comprising said amphetamine covalently bonded to a single amino acid** or to a peptide comprising from 2 to 10 amino acids, whereby the blood levels of said amphetamine achieve a therapeutically effect level but said blood levels do not result in a euphoric effect."

From **paragraph [0096]**: "**The amphetamine, A, can be any of the sympathomimetic phenethylamine**

	derivatives which have central nervous system stimulant activity such as amphetamine, or any derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, **methylenedioxyamphetamine**, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-trimethoxyamphetamine, and **3,4-methylenedioxymethamphetamine**…" From **paragraph [0107]**: "Each amino acid can be any one of the L- or D-enantiomers, preferably L-enantiomers, of the naturally occurring amino acids: alanine (Ala or A), arginine (Arg or R), asparagine (Asn or N), **aspartic acid (Asp or D)**, cysteine (Cys or C), glycine (Gly or G), **glutamic acid (Glu or E**), glutamine (Gln or Q), histidine (His or H), isoleucine (Ile or I), leucine (Leu or L), **lysine (Lys or K**), methionine (Met or M), proline (Pro or P), phenylalanine (Phe or F), serine (Ser or S), **tryptophan (Trp or W)**, threonine (Thr or T), **tyrosine (Tyr or Y**), and valine (Val or V)…" 3. MAZUR (1970) "Structure-taste relation of aspartic acid amides" J. Med. Chem. Vol 13(6): 1217-1221.

Table 2 (entry 64):

TABLE II

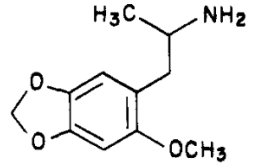
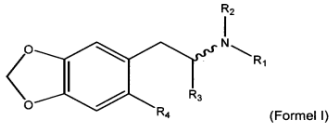
ASPARTIC ACID AMIDES
Asp-X[a]

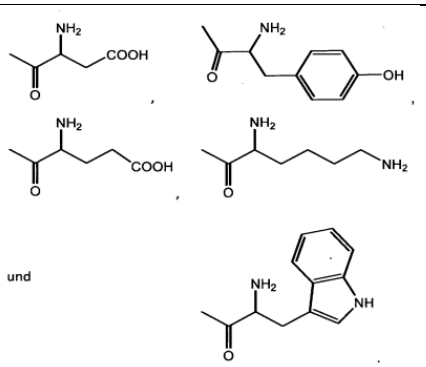
No.	X	Yield,[b] %	Mp, °C	[α]D, deg	Formula[c]	Taste
50	HNCH(CH3)CH2C6H5; L-	88 AC	197–198 W	−12 M	C13H18N2O3	50
51	HNCH(CH3)CH2C6H5; D-	98 AC	222–225 E W	+14 W	C13H18N2O3	0
52	HNCH(CH3)CH2C6H5[d]	79 M	164–166 A-W	+34 M	C13H18N2O3	-
53	HNCH2CH2C6H5	70 AC	212–214 P-W	−15 W	C12H16N2O3	0
54	HNCH(C2H5)CH2C6H5	91 AC	158–163 M-ET	+8 M	C14H20N2O3·0.25H2O	5
55	HNC(CH3)2CH2C6H5	96 AC	159–161 W	−16 M	C14H20N2O3	20
56		91 M	223–224 M-W	−6 H	C13H16N2O3	10
57	HNCHCHC6H5; L-	95 M	175–178	+5 M	C13H16N2O3·H2O	-
58	HNCH2CH(CH3)C6H5	70 AC	182–188 W	−20 W	C12H18N2O3	-
59	N(CH3)CH(CH3)CH2C6H5; L-	84 M	164–166	+47 W	C14H20N2O3·0.5H2O	-
60	N(CH3)CH(CH3)CH2C6H5; D-	82 M	185–187	+12 W	C14H20N2O3·0.5H2O	-
61	HNCH(CH3)CH2CH2C6H5	95 AC	190–196 M-W	+16 H	C13H18N2O3	5
62	HNCH(CH3)CH2OC6H5	68 M	180–184 M-W	+11 H	C12H16N2O3	10
63	HNCH2CH2OC6H5	85 AC	184–185 W	−13 H	C11H14N2O3	+
64	HNCH(CH3)CH2C6H3(OCH2O)-3,4	95 M	189–192	+6 M	C13H16N2O5	-
65	HNCH(CH2OH)CH2C6H5; L-	95 AC	237–238 W	−26 AC	C13H18N2O3	+
66	HNCH(CH3)CH(OH)C6H5	98 M	188–190 M	+10 M	C13H18N2O3·0.5H2O	+
67	HNCH(CH3)CH2C6H4OH-4	95 M	160–185	+5 W	C13H18N2O3	+
68	HNCH2CH2C6H4OH-4	72 AC	209–210 W	−21 W	C12H16N2O3	+
69	HNCH(CH2OH)CH2C6H4OH-4; L-	44 M	212–213 M	−10 H	C13H18N2O3	+
70	HNCH(CH3)CH2C6H4NHSO2CH3-4; L-	96 M	199–208 W	+14 H	C13H19N3O4S	-
71	HNCH(CH3)CH2C6H4F-4	87 M	203–209 M-ET	+9 H	C13H17FN2O3	20
72	HNCH2CH2C6H4F-4	74 M	208–209 W	−6 M	C12H15FN2O3	5
73		85 M	168–180 M-ET	+6 H	C11H16N2O3·0.333H2O	10
74		71 M	195–196 M	−17 M	C10H14N2O3	+
75		96 AC	203–205 M	−22 M	C15H19N3O3	-
76	HNCH(CH3)CH2-c-C6H11; L-	84 AC	184–185 M-W	−19 M	C13H24N2O3	50
77	HNCH(CH3)CH2-c-C6H11; D-	60 M	207–208 M-W	+16 M	C13H24N2O3	5
78	HNCH2CH2-c-C6H11	94 AC	193–202 M-W	+7 AC	C12H22N2O3	10
79	N(CH3)CH(CH3)CH2-c-C6H11; L-	78 M	179–180 P-ET	−14 W	C14H26N2O3·0.25H2O	-
80	N(CH3)CH(CH3)CH2-c-C6H11; D-	64 M	194–196	+1 W	C14H26N2O3	-
81	HN-c-C6H11	91 M	224–227 W	+16 H	C10H18N2O3	-
82	HNCH(CH3)CH2CH2CH3	92 M	190–194 A-W	+9 AC	C7H14N2O3·0.5H2O	0
83	HN(CH2)3CH(CH3)CH3	89 M	222–223 M-W		C10H20N2O3	0
84	HNCH(CH3)CH2CH(CH3)CH3; L-	91 AC	168–168 W	−17 M	C10H20N2O3·0.5H2O	-
85	HNCH(CH3)CH2CH(CH3)CH3; D-	92 AC	201–202 W	+9 M	C10H20N2O3·0.25H2O	-
86	HNCH(C2H5)CH2CH2CH3	93 M	196–200 A-W	+12 AC	C10H20N2O3·H2O	-
87	HN(CH2)3CH3	88 M	200–201 W	+9 AC	C10H20N2O3·0.25H2O	+
88	HNCH(CH3)(CH2)3CH3	98 M	188–193 A-W	+11 AC	C10H20N2O3·0.5H2O	30
89	HN(CH2)4CH3	89 M	200–201 W	+8 AC	C11H22N2O3·0.25H2O	+
90	HNCH(CH3)(CH2)4CH3	95 M	190–194	+7 AC	C11H22N2O3	20
91	HNCH(CH3)CH2CH(CH3)CH2CH3	94 M	162–166 W	−2 M	C11H22N2O3·0.25H2O	+
92	HNCH(CH3)CH2CH2CH(CH3)CH3	94 M	183–188 A-W	+9 AC	C11H22N2O3·0.25H2O	50
93	HNCH(C2H5)(CH2)2CH3	98 M	190–195	+9 AC	C11H22N2O3·0.5H2O	+
94	HNCH(CH3)(CH2)4CH3; L-	94 M	187–189 W	−5 M	C11H22N2O3·H2O	50
95	HNCH(CH3)(CH2)4CH3; L[d]	97 M	213–214 M-W	−5 M	C11H22N2O3·0.5H2O	-
96	HNCH(CH3)(CH2)4CH3; D-	96 M	217–218 M-W	+5 M	C11H22N2O3	0
97	HNCH(CH3)(CH2)4CH3; D[d]	97 M	189–192 W	+6 M	C11H22N2O3	-
98	HNCH(CH3)CH2CH2CH(CH3)CH3; L-	84 M	187–190 W	+23 H	C11H22N2O3·0.5H2O	100
99	HNCH(CH3)CH2CH2CH(CH3)CH3; L[d]	90 M	215–216 M-W	+2 M	C11H22N2O3	0
100	HNCH(CH3)CH2CH2CH(CH3)CH3; D-	96 M	210–213 M-W	−3 M	C11H22N2O3·0.5H2O	+
101	HNCH(CH3)CH2CH2CH(CH3)CH3; D[d]	91 M	192–195 W	−26 H	C11H22N2O3·0.25H2O	-
102	HNCH(CH3)CH2CH2OCH2CH3	77 M	166–170 M-ET	+3 M	C10H20N2O4·0.25H2O	10
103	HNCH(CH3)(CH2)5CH3	85 M	180–190	−8 M	C12H24N2O3·0.5H2O	10

[a] See Table I for abbreviations and explanations. [b] The amide was derived from L-Glu. [c] The amide was derived from DL-Asp. [d] The amide was derived from D-Asp. [e] All compounds were analyzed for C, H, N.

4. Gatch (2016) “Locomotor, discriminative stimulus, and place conditioning effects of MDAI in rodents” Behavioral Pharmacology, Vol 27 (6): 497-505.

From **abstract**: “5,6-Methylenedioxy-2-aminoindane (MDAI) has become a common substitute for (±)-3,4-methylenedioxymethamphetamine (MDMA) in Ecstasy. **MDAI is known to produce MDMA-like discriminative stimulus effects**, but it is not known whether MDAI has psychostimulant or hallucinogen-like effects. MDAI was tested for locomotor stimulant effects in mice and subsequently for discriminative stimulus effects in rats trained to discriminate cocaine (10 mg/kg, intraperitoneally), methamphetamine (1 mg/kg, intraperitoneally), ±MDMA (1.5 mg/kg, intraperitoneally), or (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride

	(0.5 mg/kg, intraperitoneally) from saline…MDAI fully substituted for the discriminative stimulus effects of MDMA (2.5 mg/kg), (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride (5 mg/kg), and cocaine (7.5 mg/kg), but produced only 73% methamphetamine-appropriate responding at a dose that suppressed responding (7.5 mg/kg). MDAI produced tremors at 10 mg/kg in one methamphetamine-trained rat. MDAI produced conditioned place preference from 0.3 to 10 mg/kg. **The effects of MDAI on locomotor activity and drug discrimination were similar to those produced by MDMA, having both psychostimulant-like and hallucinogen-like effects**; thus, MDAI may have similar abuse potential as MDMA. 5. Nichols (1986) "Synthesis and Evaluation of 2,3-Dihydrobenzofuran Analogues of the Hallucinogen 1-(2,5-Dimethoxy-4methylphenyl)-2-aminopropane: Drug Discrimination Studies in Rats" Vol. 29 (2): 302-304. From **page 304, paragraph 2**: "This is all the more difficult to explain in light of the fact that 2-methoxy-4,5-(methylenedioxy)amphetamine (8; MMDA-2) is active  8 and produces clear central effects at an oral dosage of 25 mg of the hydrochloride"
2. The compound of claim 1, wherein R_2 is -H, R_3 is -CH_3, and R_4 is -H.	*From the application of interest's priority document DE 10 2020 123 793.6 (filed 11 September 2020):* From **claim 1**: "1. 3,4-methylenedioxy-amphetamine peptide according to general formula I:  (Formel I) where R1 is selected from the group consisting of:



where R2 is selected from the group consisting of:
-H or -CH3.
where R3 is selected from the group consisting of:
-CH3 or -CH2-R4
where R4 is selected from the group consisting of:
-H, -OCH3, or R3-CH2-

1. US Priority Doc. No. 63/115,245 of US Pat. Doc. No. 17/518,846 "MDMA PRODRUGS TO ASSIST PSYCHOTHERAPY" (Priority doc filed 18 November 2020).

From **claim 1**: "A compound comprising a prodrug including a psychoactive base substance attached to an amino acid."

From **claim 3**: "The compound of claim 2, wherein the MDMA or MDMA-like substance is chosen from the group consisting of **MDA**…MDAI…mixed dopaminergic-serotonergic amphetamine and their N-alkylated analogs..."

From **claim 4**: "The compound of claim 1, wherein said amino acid is chosen from the group consisting of lysine, alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine."

From **claim 5**: "The compound of claim 1, wherein the amino acid is chosen from the group consisting of natural or synthetic."

Figure 1A:

Fig. 1A

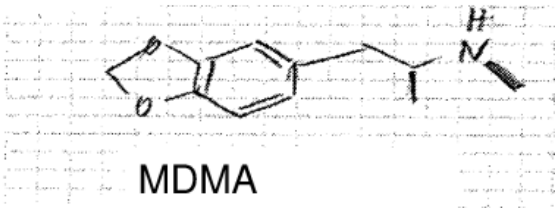
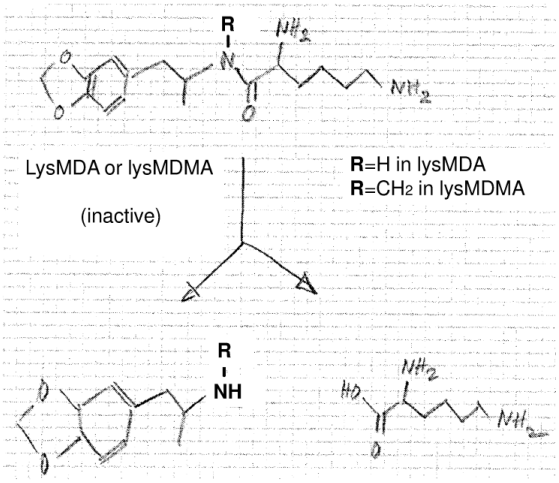


Figure 2:

Fig. 2



2. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009).

From **claim 1**: "A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt thereof, said method comprising orally administering to said subject a prodrug or a salt thereof said **prodrug comprising said amphetamine covalently bonded to a single amino acid** or to a peptide comprising from 2 to 10 amino acids, whereby the blood levels of said amphetamine achieve a therapeutically effect level but said blood levels do not result in a euphoric effect."

From **paragraph [0096]**: "The amphetamine, A, can be any of the sympathomimetic phenethylamine derivatives which have central nervous system stimulant activity such as amphetamine, or any derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, **methylenedioxyamphetamine**, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-

	trimethoxyamphetamine, and **3,4-**methylenedioxymethamphetamine…" From **paragraph [0107]**: "Each amino acid can be any one of the L- or D-enantiomers, preferably L-enantiomers, of the naturally occurring amino acids: alanine (Ala or A), arginine (Arg or R), asparagine (Asn or N), **aspartic acid (Asp or D)**, cysteine (Cys or C), glycine (Gly or G), **glutamic acid (Glu or E)**, glutamine (Gln or Q), histidine (His or H), isoleucine (Ile or I), leucine (Leu or L), **lysine (Lys or K)**, methionine (Met or M), proline (Pro or P), phenylalanine (Phe or F), serine (Ser or S), **tryptophan (Trp or W)**, threonine (Thr or T), **tyrosine (Tyr or Y)**, and valine (Val or V)…" 3. MAZUR (1970) "Structure-taste relation of aspartic acid amides" J. Med. Chem. Vol 13(6): 1217-1221.

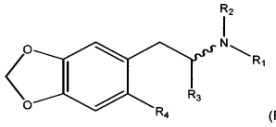
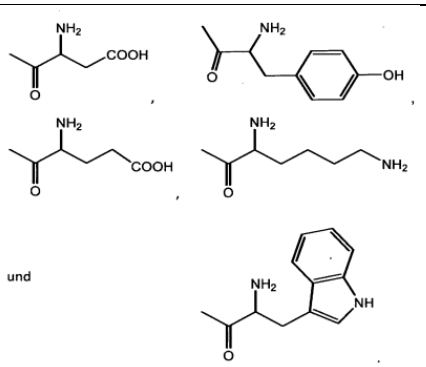
	Table 2 (entry 64):
3. The compound of claim 1, wherein R_2 is -CH_3, R_3 is -CH_3, and R_4 is -H.	*From the application of interest's priority document DE 10 2020 123 793.6 (filed 11 September 2020):* From **claim 1**: "1. 3,4-methylenedioxy-amphetamine peptide according to general formula I:  (Formel I) where R1 is selected from the group consisting of:

TABLE II

ASPARTIC ACID AMIDES Asp-X[a]

No.	X	Yield, %	Mp, °C	[α]D, deg	Formula[c]	Taste
50	HNCH(CH$_3$)CH$_2$C$_6$H$_5$; L-	88 AC	197–198 W	−12 M	$C_{13}H_{18}N_2O_3$	50
51	HNCH(CH$_3$)CH$_2$C$_6$H$_5$; D-	98 AC	222–225 E-W	+14 W	$C_{13}H_{18}N_2O_3$	0
52	HNCH(CH$_3$)CH$_2$C$_6$H$_5$[b]	79 M	164–166 A-W	+34 M	$C_{13}H_{18}N_2O_3$	-
53	HNCH$_2$CH$_2$C$_6$H$_5$	70 AC	212–214 P-W	−15 W	$C_{12}H_{16}N_2O_3$	0
54	HNCH(C$_6$H$_5$)CH$_2$C$_6$H$_5$	91 AC	158–163 M-ET	+8 M	$C_{19}H_{20}N_2O_3 \cdot 0.25H_2O$	5
55	HNC(CH$_3$)$_2$CH$_2$C$_6$H$_5$	96 AC	159–161 W	−16 M	$C_{14}H_{20}N_2O_3$	20
56		91 M	223–224 M-W	−6 H	$C_{14}H_{18}N_2O_3$	10
57	HNCHCHC$_6$H$_5$; L-	95 M	175–178	+5 M	$C_{12}H_{16}N_2O_3 \cdot H_2O$	-
58	HNCH$_2$CH(CH$_3$)C$_6$H$_5$	70 AC	182–188 W	−20 W	$C_{12}H_{18}N_2O_3$	-
59	N(CH$_3$)CH(CH$_3$)CH$_2$C$_6$H$_5$; L-	84 M	164–166	+47 W	$C_{14}H_{20}N_2O_3 \cdot 0.5H_2O$	-
60	N(CH$_3$)CH(CH$_3$)CH$_2$C$_6$H$_5$; D-	82 M	185–187	+12 W	$C_{14}H_{20}N_2O_3 \cdot 0.5H_2O$	-
61	HNCH(CH$_3$)CH$_2$CH$_2$C$_6$H$_5$	95 AC	190–196 M-W	+16 H	$C_{14}H_{20}N_2O_3$	5
62	HNCH(CH$_3$)CH$_2$OC$_6$H$_5$	68 M	180–184 M-W	+11 H	$C_{13}H_{18}N_2O_4$	10
63	HNCH$_2$CH$_2$OC$_6$H$_5$	85 AC	184–185 W	−13 H	$C_{12}H_{16}N_2O_4$	+
64	HNCH(CH$_3$)CH$_2$C$_6$H$_3$(OCH$_3$)-3,4	95 M	189–192	+6 M	$C_{15}H_{22}N_2O_4$	-
65	HNCH(CH$_2$OH)CH$_2$C$_6$H$_5$; L-	95 AC	237–238 W	−26 AC	$C_{13}H_{18}N_2O_3$	+
66	HNCH(CH$_3$)CH(OH)C$_6$H$_5$	98 M	188–190 M	+10 M	$C_{13}H_{18}N_2O_3 \cdot 0.5H_2O$	+
67	HNCH(CH$_3$)CH$_2$C$_6$H$_4$OH-4	95 M	160–185	+5 W	$C_{13}H_{18}N_2O_3$	+
68	HNCH$_2$CH$_2$C$_6$H$_4$OH-4	72 AC	209–210 W	−24 W	$C_{12}H_{16}N_2O_3$	+
69	HNCH(CH$_2$OH)CH$_2$C$_6$H$_4$OH-4; L-	44 M	212–213 M	−10 H	$C_{13}H_{18}N_2O_4$	+
70	HNCH(CH$_3$)CH$_2$C$_6$H$_4$NHSO$_2$CH$_3$-4; L-	96 M	199–208 W	+14 H	$C_{13}H_{21}N_3O_4S$	-
71	HNCH(CH$_3$)CH$_2$C$_6$H$_4$F-4	87 M	203–209 M-ET	+9 H	$C_{13}H_{17}FN_2O_3$	20
72	HNCH$_2$CH$_2$C$_6$H$_4$F-4	74 M	208–209 W	−6 M	$C_{12}H_{15}FN_2O_3$	5
73		85 M	168–180 M-ET	+6 H	$C_{11}H_{16}N_2O_4 \cdot 0.333H_2O$	10
74		71 M	195–196 M	−17 M	$C_9H_{14}N_2O_3$	+
75		96 AC	203–205 M	−22 M	$C_{15}H_{19}N_3O_3$	-
76	HNCH(CH$_3$)CH$_2$-c-C$_6$H$_{11}$; L-	84 AC	184–185 M-W	−19 M	$C_{13}H_{24}N_2O_3$	50
77	HNCH(CH$_3$)CH$_2$-c-C$_6$H$_{11}$; D-	60 M	207–208 M-W	+16 M	$C_{13}H_{24}N_2O_3$	5
78	HNCH$_2$CH$_2$-c-C$_6$H$_{11}$	94 AC	193–202 M-W	+7 AC	$C_{12}H_{22}N_2O_3$	10
79	N(CH$_3$)CH(CH$_3$)CH$_2$-c-C$_6$H$_{11}$; L-	78 M	179–180 P-ET	−14 W	$C_{14}H_{26}N_2O_3 \cdot 0.25H_2O$	-
80	N(CH$_3$)CH(CH$_3$)CH$_2$-c-C$_6$H$_{11}$; D-	64 M	194–196	+1 W	$C_{14}H_{26}N_2O_3$	-
81	HN-c-C$_6$H$_{11}$	91 M	224–227 W	+16 H	$C_{10}H_{18}N_2O_3$	-
82	HNCH(CH$_3$)CH$_2$CH$_2$CH$_3$	92 M	190–194 A-W	+9 AC	$C_{11}H_{22}N_2O_3 \cdot 0.5H_2O$	0
83	HN(CH$_2$)$_5$CH(CH$_3$)CH$_3$	89 M	222–223 M-W		$C_{16}H_{32}N_2O_3$	0
84	HNCH(CH$_3$)CH$_2$CH(CH$_3$)CH$_3$; L-	91 AC	168–168 W	−17 M	$C_{16}H_{28}N_2O_3 \cdot 0.5H_2O$	-
85	HNCH(CH$_3$)CH$_2$CH(CH$_3$)CH$_3$; D-	92 AC	201–202 W	+9 M	$C_{16}H_{28}N_2O_3 \cdot 0.25H_2O$	-
86	HNCH(C$_2$H$_5$)CH$_2$CH$_2$CH$_3$	93 M	196–200 A-W	+12 AC	$C_{16}H_{28}N_2O_3 \cdot H_2O$	-
87	HN(CH$_2$)$_5$CH$_3$	88 M	200–201 W	+9 AC	$C_{16}H_{28}N_2O_3 \cdot 0.25H_2O$	+
88	HNCH(CH$_3$)(CH$_2$)$_5$CH$_3$	98 M	188–193 A-W	+11 AC	$C_{16}H_{28}N_2O_3 \cdot 0.5H_2O$	30
89	HN(CH$_2$)$_6$CH$_3$	89 M	200–201 W	+8 AC	$C_{17}H_{32}N_2O_3 \cdot 0.25H_2O$	+
90	HNCH(CH$_3$)(CH$_2$)$_6$CH$_3$	95 M	190–194	+7 AC	$C_{17}H_{32}N_2O_3$	20
91	HNCH(CH$_3$)CH$_2$CH(CH$_3$)CH$_2$CH$_3$	94 M	162–166 W	−2 M	$C_{17}H_{32}N_2O_3 \cdot 0.25H_2O$	+
92	HNCH(CH$_3$)CH$_2$CH$_2$CH(CH$_3$)CH$_3$	94 M	183–188 A-W	+9 AC	$C_{17}H_{32}N_2O_3 \cdot 0.25H_2O$	50
93	HNCH(C$_2$H$_5$)(CH$_2$)$_3$CH$_3$	98 M	190–195	+9 AC	$C_{17}H_{32}N_2O_3 \cdot 0.5H_2O$	+
94	HNCH(CH$_3$)(CH$_2$)$_6$CH$_3$; L-	94 M	187–189 W	−5 M	$C_{17}H_{32}N_2O_3 \cdot H_2O$	50
95	HNCH(CH$_3$)(CH$_2$)$_6$CH$_3$; L[d]	97 M	213–214 M-W	−5 M	$C_{17}H_{32}N_2O_3 \cdot 0.5H_2O$	-
96	HNCH(CH$_3$)(CH$_2$)$_6$CH$_3$; D-	96 M	217–218 M-W	+5 M	$C_{17}H_{32}N_2O_3$	0
97	HNCH(CH$_3$)(CH$_2$)$_6$CH$_3$; D[d]	97 M	189–192 W	+6 M	$C_{17}H_{32}N_2O_3$	-
98	HNCH(CH$_3$)CH$_2$CH$_2$CH(CH$_3$)CH$_3$; L-	84 M	187–190 W	+23 H	$C_{17}H_{32}N_2O_3 \cdot 0.5H_2O$	100
99	HNCH(CH$_3$)CH$_2$CH$_2$CH(CH$_3$)CH$_3$; L[d]	90 M	215–216 M-W	+2 M	$C_{17}H_{32}N_2O_3$	0
100	HNCH(CH$_3$)CH$_2$CH$_2$CH(CH$_3$)CH$_3$; D-	96 M	210–213 M-W	−3 M	$C_{17}H_{32}N_2O_3 \cdot 0.5H_2O$	+
101	HNCH(CH$_3$)CH$_2$CH$_2$CH(CH$_3$)CH$_3$; D[d]	91 M	192–195 W	−26 H	$C_{17}H_{32}N_2O_3 \cdot 0.25H_2O$	-
102	HNCH(CH$_3$)CH$_2$CH$_2$OCH$_2$CH$_3$	77 M	166–170 M-ET	+3 M	$C_{16}H_{30}N_2O_4 \cdot 0.25H_2O$	10
103	HNCH(CH$_3$)(CH$_2$)$_4$CH$_3$	85 M	180–190	−8 M	$C_{17}H_{34}N_2O_3 \cdot 0.5H_2O$	10

[a] See Table I for abbreviations and explanations. [b] The amide was derived from L-Glu. [c] The amide was derived from DL-Asp. [d] The amide was derived from D-Asp. [e] All compounds were analyzed for C, H, N.



where R2 is selected from the group consisting of:
-H or -CH3.
where R3 is selected from the group consisting of:
-CH3 or -CH2-R4
where R4 is selected from the group consisting of:
-H, -OCH3, or R3-CH2-

1. US Priority Doc. No. 63/115,245 of US Pat. Doc. No. 17/518,846 "MDMA PRODRUGS TO ASSIST PSYCHOTHERAPY" (Priority doc filed 18 November 2020).

From **claim 1**: "A compound comprising a prodrug including a psychoactive base substance attached to an amino acid."

From **claim 3**: "The compound of claim 2, wherein the **MDMA** or MDMA-like substance is chosen from the group consisting of MDA…MDAI…mixed dopaminergic-serotonergic amphetamine and their N-alkylated analogs..."

From **claim 4**: "The compound of claim 1, wherein said amino acid is chosen from the group consisting of lysine, alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine."

From **claim 5**: "The compound of claim 1, wherein the amino acid is chosen from the group consisting of natural or synthetic."

Figure 1A:

Fig. 1A

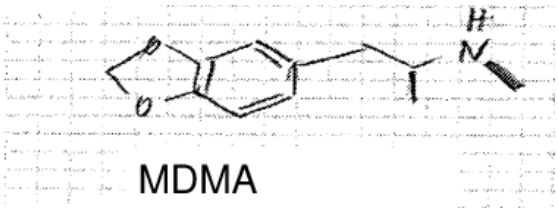
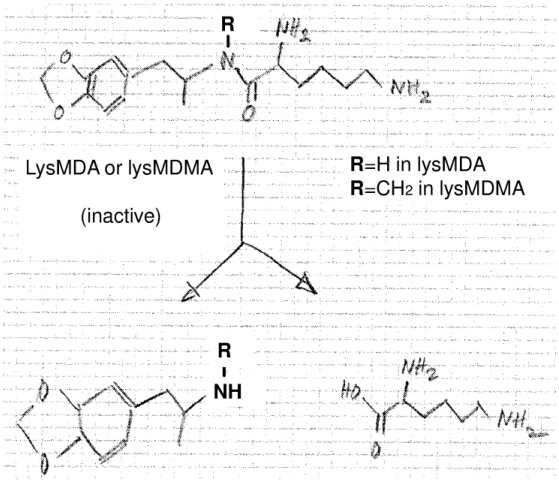


Figure 2:

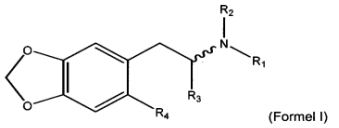
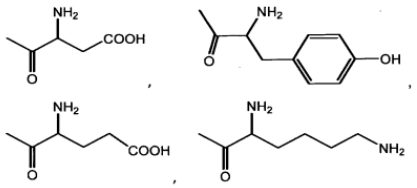
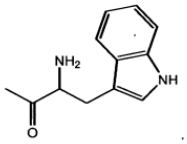
Fig. 2



2. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009).

From **claim 1**: "A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt thereof, said method comprising orally administering to said subject a prodrug or a salt thereof said **prodrug comprising said amphetamine covalently bonded to a single amino acid** or to a peptide comprising from 2 to 10 amino acids, whereby the blood levels of said amphetamine achieve a therapeutically effect level but said blood levels do not result in a euphoric effect."

From **paragraph [0096]**: "The amphetamine, A, can be any of the sympathomimetic phenethylamine derivatives which have central nervous system stimulant activity such as amphetamine, or any derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, methylenedioxyamphetamine, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-

	trimethoxyamphetamine, and **3,4-methylenedioxymethamphetamine**…" From **paragraph [0107]**: "Each amino acid can be any one of the L- or D-enantiomers, preferably L-enantiomers, of the naturally occurring amino acids: alanine (Ala or A), arginine (Arg or R), asparagine (Asn or N), **aspartic acid (Asp or D)**, cysteine (Cys or C), glycine (Gly or G), **glutamic acid (Glu or E)**, glutamine (Gln or Q), histidine (His or H), isoleucine (Ile or I), leucine (Leu or L), **lysine (Lys or K)**, methionine (Met or M), proline (Pro or P), phenylalanine (Phe or F), serine (Ser or S), **tryptophan (Trp or W)**, threonine (Thr or T), **tyrosine (Tyr or Y)**, and valine (Val or V)…"
4. The compound of claim 1, wherein R_2 is -H, R_3 is -CH_3, and R_4 is -OCH_3.	*From the application of interest's priority document DE 10 2020 123 793.6 (filed 11 September 2020):* From **claim 1**: "1. 3,4-methylenedioxy-amphetamine peptide according to general formula I:  (Formel I) where R1 is selected from the group consisting of:  und  where R2 is selected from the group consisting of: -H or -CH3. where R3 is selected from the group consisting of: -CH3 or -CH2-R4 where R4 is selected from the group consisting of: -H, -OCH3, or R3-CH2- 1. US Priority Doc. No. 63/115,245 of US Pat. Doc. No. 17/518,846 "MDMA PRODRUGS TO ASSIST PSYCHOTHERAPY" (Priority doc filed 18 November 2020). From **claim 1**: "A compound comprising a prodrug including a psychoactive base substance attached to an amino acid."

From **claim 3**: "The compound of claim 2, wherein the MDMA or MDMA-like substance is chosen from the group consisting of MDA…MDAI…**mixed dopaminergic-serotonergic amphetamine and their N-alkylated analogs**..."

From **claim 4**: "The compound of claim 1, wherein said amino acid is chosen from the group consisting of lysine, alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine."

From **claim 5**: "The compound of claim 1, wherein the amino acid is chosen from the group consisting of natural or synthetic."

Figure 1A:

Fig. 1A

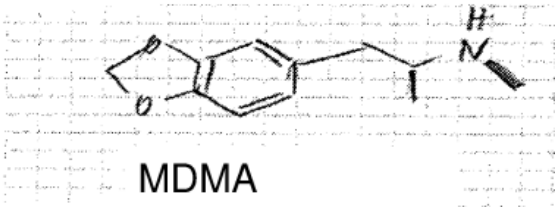
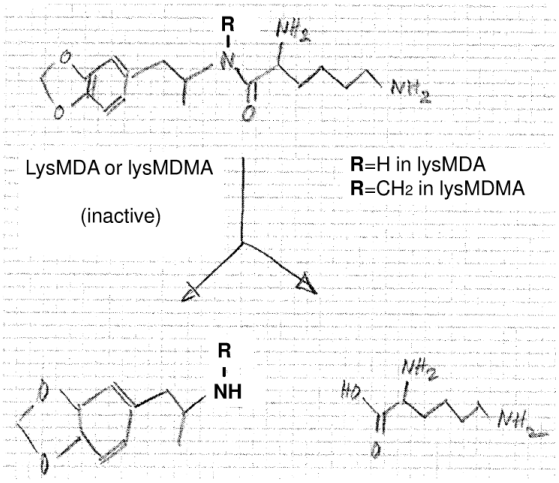


Figure 2:

Fig. 2



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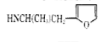
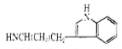
	From **claim 1**: "A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt thereof, said method comprising orally administering to said subject a prodrug or a salt thereof said **prodrug comprising said amphetamine covalently bonded to a single amino acid** or to a peptide comprising from 2 to 10 amino acids, whereby the blood levels of said amphetamine achieve a therapeutically effect level but said blood levels do not result in a euphoric effect." From **paragraph [0096]**: "**The amphetamine, A, can be any of the sympathomimetic phenethylamine derivatives which have central nervous system stimulant activity** such as amphetamine, or any derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, methylenedioxyamphetamine, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-trimethoxyamphetamine, and **3,4-**methylenedioxymethamphetamine…" From **paragraph [0107]**: "Each amino acid can be any one of the L- or D-enantiomers, preferably L-enantiomers, of the naturally occurring amino acids: alanine (Ala or A), arginine (Arg or R), asparagine (Asn or N), **aspartic acid (Asp or D)**, cysteine (Cys or C), glycine (Gly or G), **glutamic acid (Glu or E)**, glutamine (Gln or Q), histidine (His or H), isoleucine (Ile or I), leucine (Leu or L), **lysine (Lys or K)**, methionine (Met or M), proline (Pro or P), phenylalanine (Phe or F), serine (Ser or S), **tryptophan (Trp or W)**, threonine (Thr or T), **tyrosine (Tyr or Y)**, and valine (Val or V)…" 3. MAZUR (1970) "Structure-taste relation of aspartic acid amides" J. Med. Chem. Vol 13(6): 1217-1221.

Table 2 (entry 64):

TABLE II

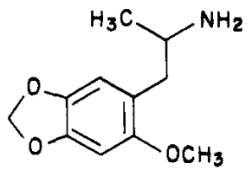
ASPARTIC ACID AMIDES Asp-X[a]

No.	X	Yield,[b] %	Mp, °C	[α]D, deg	Formula[c]	Taste
50	HNCH(CH$_3$)CH$_2$C$_6$H$_5$; L-	88 AC	197–198 W	−12 M	$C_{13}H_{18}N_2O_3$	50
51	HNCH(CH$_3$)CH$_2$C$_6$H$_5$; D-	98 AC	222–225 E-W	+14 W	$C_{13}H_{18}N_2O_3$	0
52	HNCH(CH$_3$)CH$_2$C$_6$H$_5$[d]	79 M	164–166 A-W	+34 M	$C_{13}H_{18}N_2O_3$	-
53	HNCH$_2$CH$_2$C$_6$H$_5$	70 AC	212–214 P-W	−15 W	$C_{12}H_{16}N_2O_3$	0
54	HNCH(C$_2$H$_5$)CH$_2$C$_6$H$_5$	91 AC	158–163 M-ET	+8 M	$C_{14}H_{20}N_2O_3$·0.25H$_2$O	5
55	HNC(CH$_3$)$_2$CH$_2$C$_6$H$_5$	96 AC	159–161 W	−16 M	$C_{14}H_{20}N_2O_3$	20
56		91 M	223–224 M-W	−6 H	$C_{13}H_{16}N_2O_3$	10
57	HNCHCHC$_6$H$_5$; L-	95 M	175–178	+5 M	$C_{12}H_{16}N_2O_3$·H$_2$O	–
58	HNCH$_2$CH(CH$_3$)C$_6$H$_5$	70 AC	182–188 W	−20 W	$C_{12}H_{18}N_2O_3$	–
59	N(CH$_3$)CH(CH$_3$)CH$_2$C$_6$H$_5$; L-	84 M	164–166	+47 W	$C_{14}H_{20}N_2O_3$·0.5H$_2$O	–
60	N(CH$_3$)CH(CH$_3$)CH$_2$C$_6$H$_5$; D-	82 M	185–187	+12 W	$C_{14}H_{20}N_2O_3$·0.5H$_2$O	–
61	HNCH(CH$_3$)CH$_2$CH$_2$C$_6$H$_5$	95 AC	190–196 M-W	+16 H	$C_{14}H_{20}N_2O_3$	5
62	HNCH(CH$_3$)CH$_2$OC$_6$H$_5$	68 M	180–184 M-W	+11 H	$C_{13}H_{18}N_2O_4$	10
63	HNCH$_2$CH$_2$OC$_6$H$_5$	85 AC	184–185 W	−13 H	$C_{12}H_{16}N_2O_4$	+
64	HNCH(CH$_3$)CH$_2$C$_6$H$_3$(OCH$_3$)-3,4	95 M	189–192	+6 M	$C_{15}H_{22}N_2O_4$	-
65	HNCH(CH$_2$OH)CH$_2$C$_6$H$_5$; L-	95 AC	237–238 W	−26 AC	$C_{13}H_{18}N_2O_3$	+
66	HNCH(CH$_3$)CH(OH)C$_6$H$_5$	98 M	188–190 M	+10 M	$C_{13}H_{18}N_2O_3$·0.5H$_2$O	+
67	HNCH(CH$_3$)CH$_2$C$_6$H$_4$OH-4	95 M	160–185	+5 W	$C_{13}H_{18}N_2O_3$	+
68	HNCH$_2$CH$_2$C$_6$H$_4$OH-4	72 AC	209–210 W	−21 W	$C_{12}H_{16}N_2O_3$	+
69	HNCH(CH$_2$OH)CH$_2$C$_6$H$_4$OH-4; L-	44 M	212–213 M	−10 H	$C_{13}H_{18}N_2O_4$	+
70	HNCH(CH$_3$)CH$_2$C$_6$H$_4$NHSO$_2$CH$_3$-4; L-	96 M	199–208 W	+14 H	$C_{13}H_{21}N_3O_4S$	–
71	HNCH(CH$_3$)CH$_2$C$_6$H$_4$F-4	87 M	203–209 M-ET	+9 H	$C_{13}H_{17}FN_2O_3$	20
72	HNCH$_2$CH$_2$C$_6$H$_4$F-4	74 M	208–209 W	−6 M	$C_{12}H_{15}FN_2O_3$	5
73		85 M	168–180 M-ET	+6 H	$C_{11}H_{16}N_2O_4$·0.333H$_2$O	10
74		71 M	195–196 M	−17 M	$C_9H_{14}N_2O_4$	+
75		96 AC	203–205 M	−22 M	$C_{15}H_{19}N_3O_3$	–
76	HNCH(CH$_3$)CH$_2$-c-C$_6$H$_{11}$; L-	84 AC	184–185 M-W	−19 M	$C_{13}H_{24}N_2O_3$	50
77	HNCH(CH$_3$)CH$_2$-c-C$_6$H$_{11}$; D-	60 M	207–208 M-W	+16 M	$C_{13}H_{24}N_2O_3$	5
78	HNCH$_2$CH$_2$-c-C$_6$H$_{11}$	94 AC	193–202 M-W	+7 AC	$C_{12}H_{22}N_2O_3$	10
79	N(CH$_3$)CH(CH$_3$)CH$_2$-c-C$_6$H$_{11}$; L-	78 M	179–180 P-ET	−14 W	$C_{14}H_{26}N_2O_3$·0.25H$_2$O	–
80	N(CH$_3$)CH(CH$_3$)CH$_2$-c-C$_6$H$_{11}$; D-	64 M	194–196	+1 W	$C_{14}H_{26}N_2O_3$	–
81	HN-c-C$_6$H$_{11}$	91 M	224–227 W	+16 H	$C_{10}H_{18}N_2O_3$	–
82	HNCH(CH$_3$)CH$_2$CH$_2$CH$_3$	92 M	190–194 A-W	+9 AC	$C_{11}H_{22}N_2O_3$·0.5H$_2$O	0
83	HN(CH$_2$)$_3$CH(CH$_3$)CH$_3$	89 M	222–223 M-W		$C_{10}H_{20}N_2O_3$	0
84	HNCH(CH$_3$)CH$_2$CH(CH$_3$)CH$_3$; L-	91 AC	168–168 W	−17 M	$C_{10}H_{20}N_2O_3$·0.5H$_2$O	–
85	HNCH(CH$_3$)CH$_2$CH(CH$_3$)CH$_3$; D-	92 AC	201–202 W	+9 M	$C_{10}H_{20}N_2O_3$·0.25H$_2$O	–
86	HNCH(C$_2$H$_5$)CH$_2$CH$_2$CH$_3$	93 M	196–200 A-W	+12 AC	$C_{10}H_{20}N_2O_3$·H$_2$O	–
87	HN(CH$_2$)$_3$CH$_3$	88 M	200–201 W	+9 AC	$C_{10}H_{20}N_2O_3$·0.25H$_2$O	+
88	HNCH(CH$_3$)(CH$_2$)$_3$CH$_3$	98 M	188–193 A-W	+11 AC	$C_{10}H_{20}N_2O_3$·0.5H$_2$O	30
89	HN(CH$_2$)$_4$CH$_3$	89 M	200–201 W	+8 AC	$C_{11}H_{22}N_2O_3$·0.25H$_2$O	+
90	HNCH(CH$_3$)(CH$_2$)$_4$CH$_3$	95 M	190–194	+7 AC	$C_{11}H_{22}N_2O_3$	20
91	HNCH(CH$_3$)CH$_2$CH(CH$_3$)CH$_2$CH$_3$	94 M	162–166 W	−2 M	$C_{11}H_{22}N_2O_3$·0.25H$_2$O	+
92	HNCH(CH$_3$)CH$_2$CH$_2$CH(CH$_3$)CH$_3$	94 M	183–188 A-W	+9 AC	$C_{11}H_{22}N_2O_3$·0.25H$_2$O	50
93	HNCH(C$_2$H$_5$)(CH$_2$)$_2$CH$_3$	98 M	190–195	+9 AC	$C_{11}H_{22}N_2O_3$·0.5H$_2$O	+
94	HNCH(CH$_3$)(CH$_2$)$_4$CH$_3$; L-	94 M	187–189 W	−5 M	$C_{11}H_{22}N_2O_3$·H$_2$O	50
95	HNCH(CH$_3$)(CH$_2$)$_4$CH$_3$; L[e]	97 M	213–214 M-W	−5 M	$C_{11}H_{22}N_2O_3$·0.5H$_2$O	–
96	HNCH(CH$_3$)(CH$_2$)$_4$CH$_3$; D-	96 M	217–218 M-W	+5 M	$C_{11}H_{22}N_2O_3$	0
97	HNCH(CH$_3$)(CH$_2$)$_4$CH$_3$; D[e]	97 M	189–192 W	+6 M	$C_{11}H_{22}N_2O_3$	–
98	HNCH(CH$_3$)CH$_2$CH$_2$CH(CH$_3$)CH$_3$; L-	84 M	187–190 W	+23 H	$C_{11}H_{22}N_2O_3$·0.5H$_2$O	100
99	HNCH(CH$_3$)CH$_2$CH$_2$CH(CH$_3$)CH$_3$; L[e]	90 M	215–216 M-W	+2 M	$C_{11}H_{22}N_2O_3$	0
100	HNCH(CH$_3$)CH$_2$CH$_2$CH(CH$_3$)CH$_3$; D-	96 M	210–213 M-W	−3 M	$C_{11}H_{22}N_2O_3$·0.5H$_2$O	+
101	HNCH(CH$_3$)CH$_2$CH$_2$CH(CH$_3$)CH$_3$; D[e]	91 M	192–195 W	−26 H	$C_{11}H_{22}N_2O_3$·0.25H$_2$O	–
102	HNCH(CH$_3$)CH$_2$CH$_2$OCH$_2$CH$_3$	77 M	166–170 M-ET	+3 M	$C_{10}H_{20}N_2O_4$·0.25H$_2$O	10
103	HNCH(CH$_3$)(CH$_2$)$_5$CH$_3$	85 M	180–190	−8 M	$C_{12}H_{24}N_2O_3$·0.5H$_2$O	10

[a] See Table I for abbreviations and explanations. [b] The amide was derived from L-Glu. [c] The amide was derived from DL-Asp. [d] The amide was derived from D-Asp. [e] All compounds were analyzed for C, H, N.

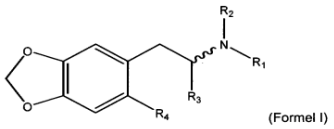
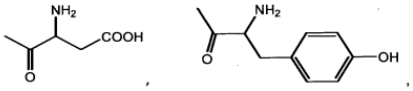
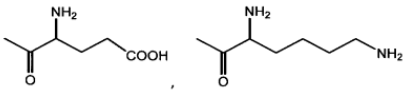
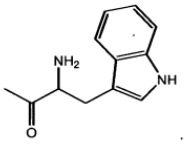
5. Nichols (1986) “Synthesis and Evaluation of 2,3-Dihydrobenzofuran Analogues of the Hallucinogen 1-(2,5-Dimethoxy-4methylphenyl)-2-aminopropane: Drug Discrimination Studies in Rats” Vol. 29 (2): 302-304.

From **page 304, paragraph 2**: “This is all the more difficult to explain in light of the fact that 2-methoxy-4,5-(methylenedioxy)amphetamine (8; MMDA-2) is active



8

and produces clear central effects at an oral dosage of 25 mg of the hydrochloride”

5. The compound of claim 1, wherein R_2 is -H, and where R_3 and R_4 are mutually joined to form a group -CH_2-.	*From the application of interest's priority document DE 10 2020 123 793.6 (filed 11 September 2020):* From **claim 1**: "1. 3,4-methylenedioxy-amphetamine peptide according to general formula I:  (Formel I) where R1 is selected from the group consisting of:   und  where R2 is selected from the group consisting of: -H or -CH3. where R3 is selected from the group consisting of: -CH3 or -CH2-R4 where R4 is selected from the group consisting of: -H, -OCH3, or R3-CH2- 1. US Priority Doc. No. 63/115,245 of US Pat. Doc. No. 17/518,846 "MDMA PRODRUGS TO ASSIST PSYCHOTHERAPY" (Priority doc filed 18 November 2020). From **claim 1**: "A compound comprising a prodrug including a psychoactive base substance attached to an amino acid." From **claim 3**: "The compound of claim 2, wherein the MDMA or MDMA-like substance is chosen from the group consisting of MDA…**MDAI**…mixed dopaminergic-serotonergic amphetamine and their N-alkylated analogs..." From **claim 4**: "The compound of claim 1, wherein said amino acid is chosen from the group consisting of lysine, alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine."

From **claim 5**: "The compound of claim 1, wherein the amino acid is chosen from the group consisting of natural or synthetic."

Figure 1A:

Fig. 1A

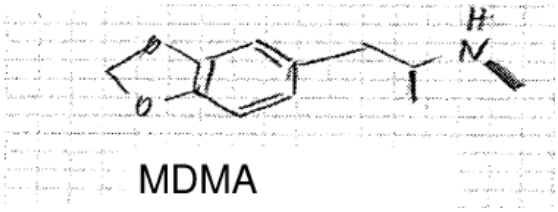
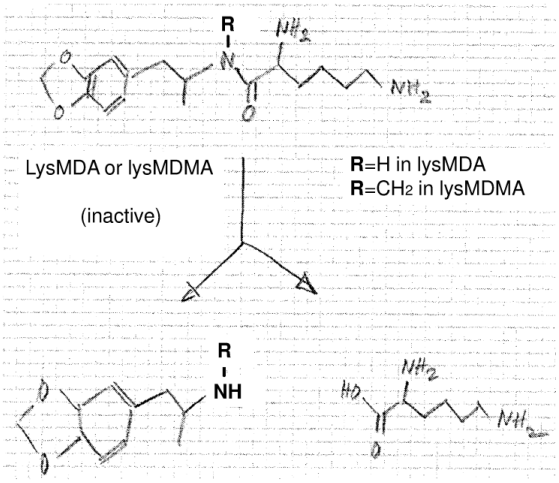


Figure 2:

Fig. 2



2. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009).

From **claim 1**: "A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt thereof, said method comprising orally administering to said subject a prodrug or a salt thereof said **prodrug comprising said amphetamine covalently bonded to a single amino acid** or to a peptide comprising from 2 to 10 amino acids, whereby the blood levels of said amphetamine achieve a therapeutically effect level but said blood levels do not result in a euphoric effect."

From **paragraph [0096]**: "**The amphetamine, A, can be any of the sympathomimetic phenethylamine derivatives which have central nervous system stimulant activity** such as amphetamine, or any

	derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, methylenedioxyamphetamine, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-trimethoxyamphetamine, and 3,4-methylenedioxymethamphetamine…" From **paragraph [0107]**: "Each amino acid can be any one of the L- or D-enantiomers, preferably L-enantiomers, of the naturally occurring amino acids: alanine (Ala or A), arginine (Arg or R), asparagine (Asn or N), **aspartic acid (Asp or D**), cysteine (Cys or C), glycine (Gly or G), **glutamic acid (Glu or E)**, glutamine (Gln or Q), histidine (His or H), isoleucine (Ile or I), leucine (Leu or L), **lysine (Lys or K)**, methionine (Met or M), proline (Pro or P), phenylalanine (Phe or F), serine (Ser or S), **tryptophan (Trp or W)**, threonine (Thr or T), **tyrosine (Tyr or Y),** and valine (Val or V)…" 3. MAZUR (1970) "Structure-taste relation of aspartic acid amides" J. Med. Chem. Vol 13(6): 1217-1221.

Table 2 (entry 64):

TABLE II

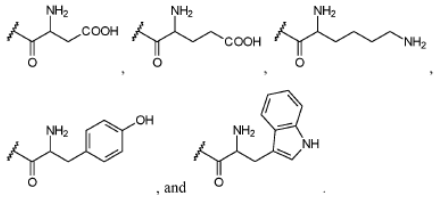
ASPARTIC ACID AMIDES
Asp-X[a]

No.	X	Yield,[b] %	Mp, °C	[α]D, deg	Formula[c]	Taste
50	HNCH(CH3)CH2C6H5; L-	88 AC	197–198 W	−12 M	C13H18N2O3	50
51	HNCH(CH3)CH2C6H5; D-	98 AC	222–225 E W	+14 W	C13H18N2O3	0
52	HNCH(CH3)CH2C6H5[d]	79 M	164–166 A-W	+34 M	C13H18N2O3	-
53	HNCH2CH2C6H5	70 AC	212–214 P-W	−15 W	C12H16N2O3	0
54	HNCH(C2H5)CH2C6H5	91 AC	158–163 M-ET	+8 M	C14H20N2O3·0.25H2O	5
55	HNC(CH3)2CH2C6H5	96 AC	159–161 W	−16 M	C14H20N2O3	20
56		91 M	223–224 M-W	−6 H	C13H16N2O3	10
57	HNCHCHC6H5; L-	95 M	175–178	+5 M	C13H16N2O3·H2O	-
58	HNCH2CH(CH3)C6H5	70 AC	182–188 W	−20 W	C12H18N2O3	-
59	N(CH3)CH(CH3)CH2C6H5; L-	84 M	164–166	+47 W	C14H20N2O3·0.5H2O	-
60	N(CH3)CH(CH3)CH2C6H5; D-	82 M	185–187	+12 W	C14H20N2O3·0.5H2O	-
61	HNCH(CH3)CH2CH2C6H5	95 AC	190–196 M-W	+16 H	C13H18N2O3	5
62	HNCH(CH3)CH2OC6H5	68 M	180–184 M-W	+11 H	C12H16N2O3	10
63	HNCH2CH2OC6H5	85 AC	184–185 W	−13 H	C11H14N2O3	+
64	HNCH(CH3)CH2C6H3(OCH2O)-3,4	95 M	189–192	+6 M	C13H16N2O5	-
65	HNCH(CH2OH)CH2C6H5; L-	95 AC	237–238 W	−26 AC	C13H18N2O3	+
66	HNCH(CH3)CH(OH)C6H5	98 M	188–190 M	+10 M	C13H18N2O3·0.5H2O	+
67	HNCH(CH3)CH2C6H4OH-4	95 M	160–185	+5 W	C13H18N2O3	+
68	HNCH2CH2C6H4OH-4	72 AC	209–210 W	−21 W	C12H16N2O3	+
69	HNCH(CH2OH)CH2C6H4OH-4; L-	44 M	212–213 M	−10 H	C13H18N2O3	+
70	HNCH(CH3)CH2C6H4NHSO2CH3-4; L-	96 M	199–208 W	+14 H	C13H19N3O4S	-
71	HNCH(CH3)CH2C6H4F-4	87 M	203–209 M-ET	+9 H	C13H17FN2O3	20
72	HNCH2CH2C6H4F-4	74 M	208–209 W	−6 M	C12H15FN2O3	5
73		85 M	168–180 M-ET	+6 H	C11H16N2O3·0.333H2O	10
74		71 M	195–196 M	−17 M	C10H14N2O3	+
75		96 AC	203–205 M	−22 M	C15H19N3O3	-
76	HNCH(CH3)CH2-c-C6H11; L-	84 AC	184–185 M-W	−19 M	C13H24N2O3	50
77	HNCH(CH3)CH2-c-C6H11; D-	60 M	207–208 M-W	+16 M	C13H24N2O3	5
78	HNCH2CH2-c-C6H11	94 AC	193–202 M-W	+7 AC	C12H22N2O3	10
79	N(CH3)CH(CH3)CH2-c-C6H11; L-	78 M	179–180 P-ET	−14 W	C14H26N2O3·0.25H2O	-
80	N(CH3)CH(CH3)CH2-c-C6H11; D-	64 M	194–196	+1 W	C14H26N2O3	-
81	HN-c-C6H11	91 M	224–227 W	+16 H	C10H18N2O3	-
82	HNCH(CH3)CH2CH2CH3	92 M	190–194 A-W	+9 AC	C7H14N2O3·0.5H2O	0
83	HN(CH2)3CH(CH3)CH3	89 M	222–223 M-W		C10H20N2O3	0
84	HNCH(CH3)CH2CH(CH3)CH3; L-	91 AC	168–168 W	−17 M	C10H20N2O3·0.5H2O	-
85	HNCH(CH3)CH2CH(CH3)CH3; D-	92 AC	201–202 W	+9 M	C10H20N2O3·0.25H2O	-
86	HNCH(C2H5)CH2CH2CH3	93 M	196–200 A-W	+12 AC	C10H20N2O3·H2O	-
87	HN(CH2)3CH3	88 M	200–201 W	+9 AC	C10H20N2O3·0.25H2O	+
88	HNCH(CH3)(CH2)3CH3	98 M	188–193 A-W	+11 AC	C10H20N2O3·0.5H2O	30
89	HN(CH2)4CH3	89 M	200–201 W	+8 AC	C11H22N2O3·0.25H2O	+
90	HNCH(CH3)(CH2)4CH3	95 M	190–194	+7 AC	C11H22N2O3	20
91	HNCH(CH3)CH2CH(CH3)CH2CH3	94 M	162–166 W	−2 M	C11H22N2O3·0.25H2O	+
92	HNCH(CH3)CH2CH2CH(CH3)CH3	94 M	183–188 A-W	+9 AC	C11H22N2O3·0.25H2O	50
93	HNCH(C2H5)(CH2)2CH3	98 M	190–195	+9 AC	C11H22N2O3·0.5H2O	+
94	HNCH(CH3)(CH2)4CH3; L-	94 M	187–189 W	−5 M	C11H22N2O3·H2O	50
95	HNCH(CH3)(CH2)4CH3; L[d]	97 M	213–214 M-W	−5 M	C11H22N2O3·0.5H2O	-
96	HNCH(CH3)(CH2)4CH3; D-	96 M	217–218 M-W	+5 M	C11H22N2O3	0
97	HNCH(CH3)(CH2)4CH3; D[d]	97 M	189–192 W	+6 M	C11H22N2O3	-
98	HNCH(CH3)CH2CH2CH(CH3)CH3; L-	84 M	187–190 W	+23 H	C11H22N2O3·0.5H2O	100
99	HNCH(CH3)CH2CH2CH(CH3)CH3; L[d]	90 M	215–216 M-W	+2 M	C11H22N2O3	0
100	HNCH(CH3)CH2CH2CH(CH3)CH3; D-	96 M	210–213 M-W	−3 M	C11H22N2O3·0.5H2O	+
101	HNCH(CH3)CH2CH2CH(CH3)CH3; D[d]	91 M	192–195 W	−26 H	C11H22N2O3·0.25H2O	-
102	HNCH(CH3)CH2CH2OCH2CH3	77 M	166–170 M-ET	+3 M	C10H20N2O4·0.25H2O	10
103	HNCH(CH3)(CH2)5CH3	85 M	180–190	−8 M	C12H24N2O3·0.5H2O	10

[a] See Table I for abbreviations and explanations. [b] The amide was derived from L-Glu. [c] The amide was derived from DL-Asp. [d] The amide was derived from D-Asp. [e] All compounds were analyzed for C, H, N.

4. Gatch (2016) “Locomotor, discriminative stimulus, and place conditioning effects of MDAI in rodents” Behavioral Pharmacology, Vol 27 (6): 497-505.

From **abstract**: “5,6-Methylenedioxy-2-aminoindane (MDAI) has become a common substitute for (±)-3,4-methylenedioxymethamphetamine (MDMA) in Ecstasy. **MDAI is known to produce MDMA-like discriminative stimulus effects**, but it is not known whether MDAI has psychostimulant or hallucinogen-like effects. MDAI was tested for locomotor stimulant effects in mice and subsequently for discriminative stimulus effects in rats trained to discriminate cocaine (10 mg/kg, intraperitoneally), methamphetamine (1 mg/kg, intraperitoneally), ±MDMA (1.5 mg/kg, intraperitoneally), or (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride

	(0.5 mg/kg, intraperitoneally) from saline…MDAI fully substituted for the discriminative stimulus effects of MDMA (2.5 mg/kg), (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride (5 mg/kg), and cocaine (7.5 mg/kg), but produced only 73% methamphetamine-appropriate responding at a dose that suppressed responding (7.5 mg/kg). MDAI produced tremors at 10 mg/kg in one methamphetamine-trained rat. MDAI produced conditioned place preference from 0.3 to 10 mg/kg. **The effects of MDAI on locomotor activity and drug discrimination were similar to those produced by MDMA, having both psychostimulant-like and hallucinogen-like effects**; thus, MDAI may have similar abuse potential as MDMA.
6. The compound of claim 1, wherein R_1 is selected from:  , and	2. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009). From **claim 1**: "A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt thereof, said method comprising orally administering to said subject a prodrug or a salt thereof said **prodrug comprising said amphetamine covalently bonded to a single amino acid** or to a peptide comprising from 2 to 10 amino acids, whereby the blood levels of said amphetamine achieve a therapeutically effect level but said blood levels do not result in a euphoric effect." From **paragraph [0096]**: "The amphetamine, A, can be any of the sympathomimetic phenethylamine derivatives which have central nervous system stimulant activity such as amphetamine, or any derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, **methylenedioxyamphetamine**, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-trimethoxyamphetamine, and **3,4-methylenedioxymethamphetamine**…" From **paragraph [0107]**: "Each amino acid can be any one of the L- or D-enantiomers, preferably L-enantiomers, of the naturally occurring amino acids: alanine (Ala or A), arginine (Arg or R), asparagine (Asn or N), **aspartic acid (Asp or D)**, cysteine (Cys or C), glycine (Gly or G), **glutamic acid (Glu or E)**, glutamine (Gln or Q), histidine (His or H), isoleucine (Ile or I), leucine (Leu or L), **lysine (Lys or K)**, methionine (Met or M), proline (Pro or P), phenylalanine (Phe or F), serine (Ser or S), **tryptophan (Trp or W**), threonine (Thr or T), **tyrosine (Tyr or Y)**, and valine (Val or V)…"

3. MAZUR (1970) “Structure-taste relation of aspartic acid amides” J. Med. Chem. Vol 13(6): 1217-1221.

Table 2 (entry 64):

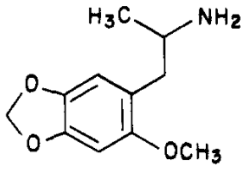
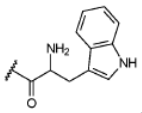
TABLE II
ASPARTIC ACID AMIDES
Asp-X

No.	X	Yield,[a] %	Mp, °C	[α]D, deg	Formula[b]	Taste
50	HNCH(CH3)CH2C6H5; L-	88 AC	197–198 W	−12 M	C13H18N2O3	50
51	HNCH(CH3)CH2C6H5; D-	98 AC	222–225 E W	+14 W	C13H18N2O3	0
52	HNCH(CH3)CH2C6H5[c]	79 M	164–166 A W	+34 M	C13H18N2O3	-
53	HNCH2CH2C6H5	70 AC	212–214 P-W	−15 W	C12H16N2O3	0
54	HNCH(C3H5)CH2C6H5	91 AC	158–163 M–ET	+8 M	C14H20N2O3·0.25H2O	5
55	HNC(CH3)2CH2C6H5	96 AC	159–161 W	−16 M	C13H20N2O3	20
56		91 M	223–224 M–W	−6 H	C14H16N2O3	10
57	HNCHCHC6H5; L-	95 M	175–178	+5 M	C13H16N2O3·H2O	–
58	HNCH2CH(CH3)C6H5	70 AC	182–188 W	−20 W	C13H18N2O3	–
59	N(CH3)CH(CH3)CH2C6H5; L-	84 M	164–166	+47 W	C14H20N2O3·0.5H2O	–
60	N(CH3)CH(CH3)CH2C6H5; D-	82 M	185–187	+12 W	C14H20N2O3·0.5H2O	–
61	HNCH(CH3)CH2CH2C6H5	95 AC	190–196 M–W	+16 H	C13H18N2O3	5
62	HNCH(CH3)CH2OC6H5	68 M	180–184 M–W	+11 H	C12H16N2O3	10
63	HNCH2CH2OC6H5	85 AC	184–185 W	−13 H	C12H16N2O3	+
64	HNCH(CH3)CH2C6H3(OCH2O)-3,4	95 M	189–192	+6 M	C13H16N2O5	–
65	HNCH(CH2OH)CH2C6H5; L-	95 AC	237–238 W	−26 AC	C13H18N2O3	+
66	HNCH(CH3)CH(OH)C6H5	98 M	188–190 M	+10 M	C13H18N2O3·0.5H2O	+
67	HNCH(CH3)CH2C6H4OH-4	95 M	160–185	+5 W	C13H18N2O3	+
68	HNCH2CH2C6H4OH-4	72 AC	209–210 W	−21 W	C12H16N2O3	+
69	HNCH(CH2OH)CH2C6H4OH-4; L-	44 M	212–213 M	−10 H	C13H18N2O3	+
70	HNCH(CH3)CH2C6H4NHSO2CH3-4; L-	96 M	199–208 W	+14 H	C14H21N3O4S	–
71	HNCH(CH3)CH2C6H4F-4	87 M	203–209 M–ET	+9 H	C13H17FN2O3	20
72	HNCH2CH2C6H4F-4	74 M	208–209 W	−6 M	C12H15FN2O3	5
73		85 M	168–180 M–ET	+6 H	C11H16N2O4·0.333H2O	10
74		71 M	195–196 M	−17 M	C10H14N2O3	+
75		96 AC	203–205 M	−22 M	C12H15N3O2	–
76	HNCH(CH3)CH2-o-C6H10; L-	84 AC	184–185 M–W	−19 M	C13H24N2O3	50
77	HNCH(CH3)CH2-o-C6H10; D-	60 M	207–208 M–W	+16 M	C13H24N2O3	5
78	HNCH2CH2-o-C6H11	94 AC	193–202 M–W	+7 AC	C13H26N2O3	10
79	N(CH3)CH(CH3)CH2-o-C6H11; L-	78 M	179–180 P–ET	−14 W	C14H28N2O3·0.25H2O	–
80	N(CH3)CH(CH3)CH2-o-C6H11; D-	64 M	194–196	+1 W	C14H28N2O3	–
81	HN-o-C6H11	91 M	224–225 W	+16 H	C10H18N2O3	–
82	HNCH(CH3)CH2CH2CH3	92 M	190–194 A W	+9 AC	C7H16N2O3·0.5H2O	0
83	HN(CH2)2CH(CH3)CH2	89 M	222–223 M–W		C10H18N2O3	0
84	HNCH(CH3)CH2CH(CH3)CH3; L-	91 AC	166–168 W	−17 M	C10H20N2O3·0.5H2O	–
85	HNCH(CH3)CH2CH(CH3)CH3; D-	92 AC	201–202 W	+9 M	C10H20N2O3·0.25H2O	–
86	HNCH(C2H5)CH2CH2CH3	93 M	196–200 A W	+12 AC	C10H20N2O3·H2O	–
87	HN(CH2)3CH3	88 M	200–201 W	+9 AC	C10H20N2O3·0.25H2O	+
88	HNCH(CH3)(CH2)3CH3	98 M	188–193 A W	+11 AC	C10H20N2O3·0.5H2O	30
89	HN(CH2)4CH3	89 M	200–201 W	+8 AC	C11H22N2O3·0.25H2O	+
90	HNCH(CH3)(CH2)4CH3	95 M	190–194	+7 AC	C11H22N2O3	20
91	HNCH(CH3)CH2CH(CH3)CH2CH3	94 M	162–166 W	−2 M	C11H22N2O3·0.25H2O	+
92	HNCH(CH3)CH2CH2CH(CH3)CH3	94 M	181–188 A–W	+9 AC	C11H22N2O3·0.25H2O	50
93	HNCH(C2H5)(CH2)3CH3	98 M	190–195	+9 AC	C11H22N2O3·0.5H2O	+
94	HNCH(CH2)(CH2)4CH3; L-	94 M	187–189 W	−5 M	C11H22N2O3·H2O	50
95	HNCH(CH3)(CH2)4CH3; L[d]	97 M	213–214 M–W	−5 M	C11H22N2O3·0.5H2O	–
96	HNCH(CH3)(CH2)4CH3; D-	96 M	217–218 M–W	+5 M	C11H22N2O3	0
97	HNCH(CH3)(CH2)4CH3; D[d]	97 M	189–192 W	+6 M	C11H22N2O3	–
98	HNCH(CH3)CH2CH2CH(CH3)CH3; L-	84 M	187–190 W	+23 H	C11H22N2O3·0.5H2O	100
99	HNCH(CH3)CH2CH2CH(CH3)CH3; L[d]	99 M	215–216 M–W	+2 M	C11H22N2O3	0
100	HNCH(CH3)CH2CH2CH(CH3)CH3; D-	96 M	210–213 M–W	−3 M	C11H22N2O3·0.5H2O	+
101	HNCH(CH3)CH2CH2CH(CH3)CH3; D[d]	91 M	192–195 W	−26 H	C11H22N2O3·0.25H2O	–
102	HNCH(CH3)CH2CH2OCH2CH3	77 M	166–170 M–ET	+3 M	C10H20N2O4·0.25H2O	10
103	HNCH(CH2)(CH2)4CH3	85 M	180–190	−8 M	C12H24N2O3·0.5H2O	10

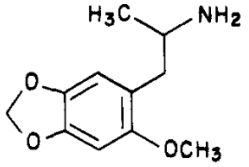
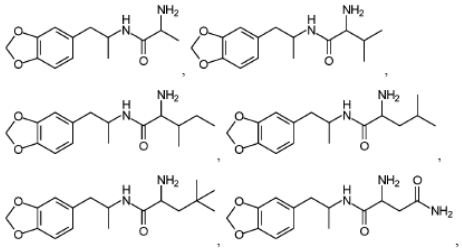
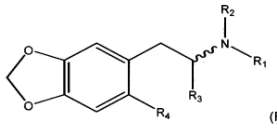
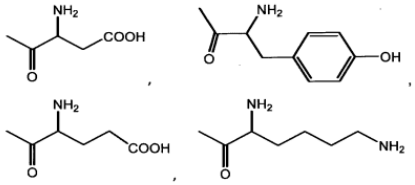
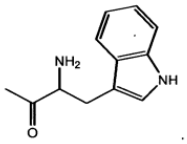
[a] See Table I for abbreviations and explanations. [b] The amide was derived from L-Glu. [c] The amide was derived from DL-Asp. [d] The amide was derived from D-Asp. [e] All compounds were analyzed for C, H, N.

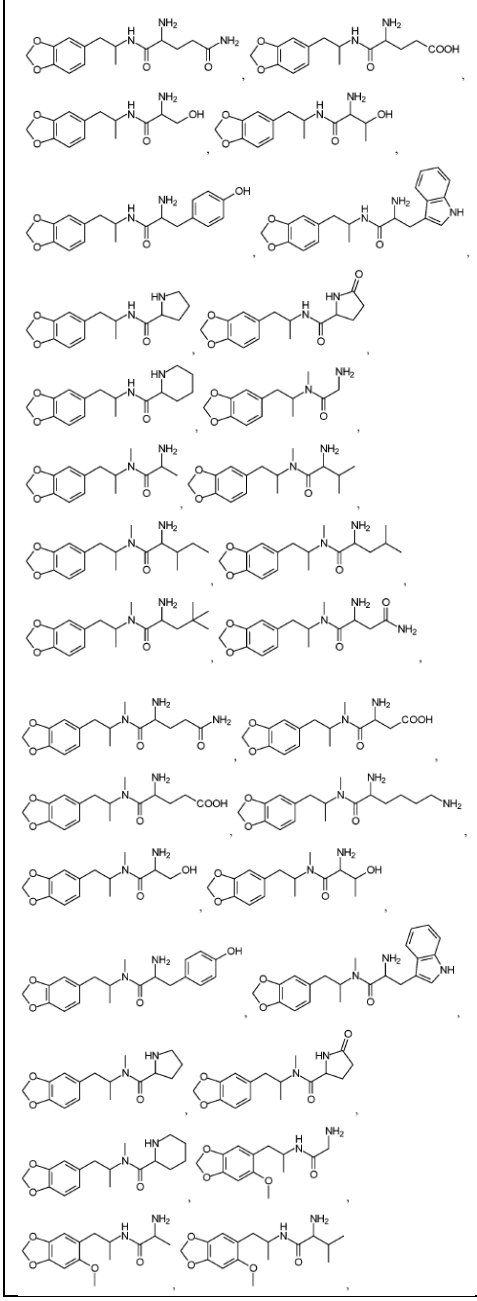
4. Gatch (2016) “Locomotor, discriminative stimulus, and place conditioning effects of MDAI in rodents” Behavioral Pharmacology, Vol 27 (6): 497-505.

From **abstract**: “5,6-Methylenedioxy-2-aminoindane (MDAI) has become a common substitute for (±)-3,4-methylenedioxymethamphetamine (MDMA) in Ecstasy. **MDAI is known to produce MDMA-like discriminative stimulus effects**, but it is not known whether MDAI has psychostimulant or hallucinogen-like effects. MDAI was tested for locomotor stimulant effects in mice and subsequently for discriminative stimulus effects in rats

	trained to discriminate cocaine (10 mg/kg, intraperitoneally), methamphetamine (1 mg/kg, intraperitoneally), ±MDMA (1.5 mg/kg, intraperitoneally), or (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride (0.5 mg/kg, intraperitoneally) from saline…MDAI fully substituted for the discriminative stimulus effects of MDMA (2.5 mg/kg), (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride (5 mg/kg), and cocaine (7.5 mg/kg), but produced only 73% methamphetamine-appropriate responding at a dose that suppressed responding (7.5 mg/kg). MDAI produced tremors at 10 mg/kg in one methamphetamine-trained rat. MDAI produced conditioned place preference from 0.3 to 10 mg/kg. **The effects of MDAI on locomotor activity and drug discrimination were similar to those produced by MDMA, having both psychostimulant-like and hallucinogen-like effects**; thus, MDAI may have similar abuse potential as MDMA. 5. Nichols (1986) "Synthesis and Evaluation of 2,3-Dihydrobenzofuran Analogues of the Hallucinogen 1-(2,5-Dimethoxy-4methylphenyl)-2-aminopropane: Drug Discrimination Studies in Rats" Vol. 29 (2): 302-304. From **page 304, paragraph 2**: "This is all the more difficult to explain in light of the fact that 2-methoxy-4,5-(methylenedioxy)amphetamine (8; MMDA-2) is active  8 and produces clear central effects at an oral dosage of 25 mg of the hydrochloride"
7. The compound of claim 1, wherein R_1 is:  	2. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009). From **claim 1**: "A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt thereof, said method comprising orally administering to said subject a prodrug or a salt thereof said **prodrug comprising said amphetamine covalently bonded to a single amino acid** or to a peptide comprising from 2 to 10 amino acids, whereby the blood levels of said amphetamine achieve a therapeutically effect level but said blood levels do not result in a euphoric effect."

	From **paragraph [0096]**: "**The amphetamine, A, can be any of the sympathomimetic phenethylamine derivatives which have central nervous system stimulant activity** such as amphetamine, or any derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, **methylenedioxyamphetamine**, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-trimethoxyamphetamine, and **3,4-methylenedioxymethamphetamine**…" From **paragraph [0107]**: "Each amino acid can be any one of the L- or D-enantiomers, preferably L-enantiomers, of the naturally occurring amino acids: alanine (Ala or A), arginine (Arg or R), asparagine (Asn or N), aspartic acid (Asp or D), cysteine (Cys or C), glycine (Gly or G), glutamic acid (Glu or E), glutamine (Gln or Q), histidine (His or H), isoleucine (Ile or I), leucine (Leu or L), lysine (Lys or K), methionine (Met or M), proline (Pro or P), phenylalanine (Phe or F), serine (Ser or S), **tryptophan (Trp or W),** threonine (Thr or T), tyrosine (Tyr or Y), and valine (Val or V)…" 4. Gatch (2016) "Locomotor, discriminative stimulus, and place conditioning effects of MDAI in rodents" Behavioral Pharmacology, Vol 27 (6): 497-505. From **abstract**: "5,6-Methylenedioxy-2-aminoindane (MDAI) has become a common substitute for (±)-3,4-methylenedioxymethamphetamine (MDMA) in Ecstasy. **MDAI is known to produce MDMA-like discriminative stimulus effects**, but it is not known whether MDAI has psychostimulant or hallucinogen-like effects. MDAI was tested for locomotor stimulant effects in mice and subsequently for discriminative stimulus effects in rats trained to discriminate cocaine (10 mg/kg, intraperitoneally), methamphetamine (1 mg/kg, intraperitoneally), ±MDMA (1.5 mg/kg, intraperitoneally), or (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride (0.5 mg/kg, intraperitoneally) from saline…MDAI fully substituted for the discriminative stimulus effects of MDMA (2.5 mg/kg), (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride (5 mg/kg), and cocaine (7.5 mg/kg), but produced only 73% methamphetamine-appropriate responding at a dose that suppressed responding (7.5 mg/kg). MDAI produced tremors at 10 mg/kg in one methamphetamine-trained rat. MDAI produced conditioned place preference from 0.3 to 10 mg/kg. **The effects of MDAI on locomotor activity and drug discrimination were similar to those**

	produced by MDMA, having both psychostimulant-like and hallucinogen-like effects; thus, MDAI may have similar abuse potential as MDMA. 5. Nichols (1986) "Synthesis and Evaluation of 2,3-Dihydrobenzofuran Analogues of the Hallucinogen 1-(2,5-Dimethoxy-4methylphenyl)-2-aminopropane: Drug Discrimination Studies in Rats" Vol. 29 (2): 302-304. From **page 304, paragraph 2**: "This is all the more difficult to explain in light of the fact that 2-methoxy-4,5-(methylenedioxy)amphetamine (8; MMDA-2) is active  8 and produces clear central effects at an oral dosage of 25 mg of the hydrochloride"
8. The compound of claim 1, wherein said compound is selected from any one of the following compounds: 	*From the application of interest's priority document DE 10 2020 123 793.6 (filed 11 September 2020):* From **claim 1**: "1. 3,4-methylenedioxy-amphetamine peptide according to general formula I:  (Formel I) where R1 is selected from the group consisting of:  und  where R2 is selected from the group consisting of: -H or -CH3. where R3 is selected from the group consisting of: -CH3 or -CH2-R4 where R4 is selected from the group consisting of: -H, -OCH3, or R3-CH2-



1. US Priority Doc. No. 63/115,245 of US Pat. Doc. No. 17/518,846 “MDMA PRODRUGS TO ASSIST PSYCHOTHERAPY” (Priority doc filed 18 November 2020).

From **claim 1**: “A compound comprising a prodrug including a psychoactive base substance attached to an amino acid.”

From **claim 3**: “The compound of claim 2, wherein the MDMA or MDMA-like substance is chosen from the group consisting of MDA…MDAI…mixed dopaminergic-serotonergic amphetamine and their N-alkylated analogs...”

From **claim 4**: “The compound of claim 1, wherein said amino acid is chosen from the group consisting of lysine, alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine.”

From **claim 5**: “The compound of claim 1, wherein the amino acid is chosen from the group consisting of natural or synthetic.”

Figure 1A:

Fig. 1A

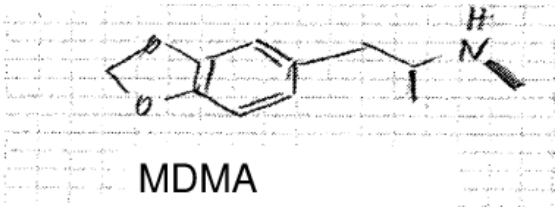
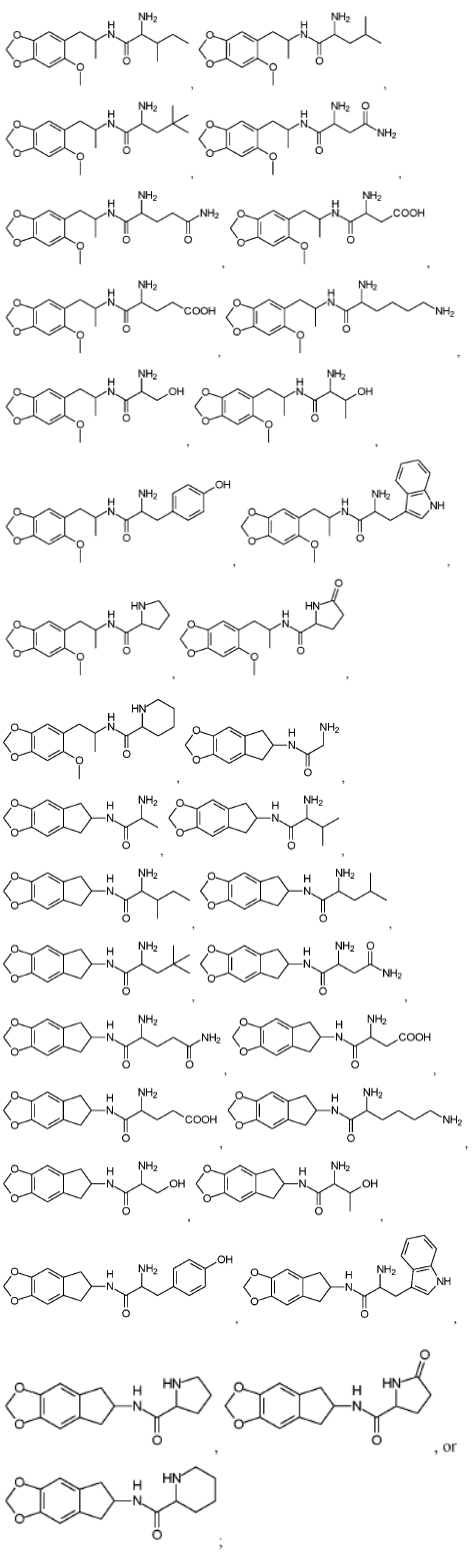


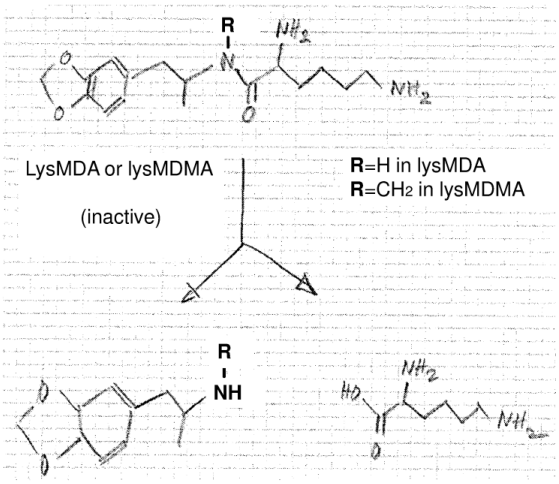
Figure 2:



, or

or a pharmaceutically acceptable salt thereof.

Fig. 2



2. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009).

From **claim 1**: "A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt thereof, said method comprising orally administering to said subject a prodrug or a salt thereof said **prodrug comprising said amphetamine covalently bonded to a single amino acid** or to a peptide comprising from 2 to 10 amino acids, whereby the blood levels of said amphetamine achieve a therapeutically effect level but said blood levels do not result in a euphoric effect."

From **paragraph [0096]**: "**The amphetamine, A, can be any of the sympathomimetic phenethylamine derivatives which have central nervous system stimulant activity** such as amphetamine, or any derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, **methylenedioxyamphetamine**, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-trimethoxyamphetamine, and **3,4-methylenedioxymethamphetamine**…"

From **paragraph [0107]**: "Each amino acid can be any one of the L- or D-enantiomers, preferably L-enantiomers, of the naturally occurring amino acids: **alanine (Ala or A)**, arginine (Arg or R), **asparagine (Asn or N)**, aspartic acid (Asp or D), cysteine (Cys or C), glycine (Gly or G), **glutamic acid (Glu or E)**, **glutamine (Gln or Q)**, histidine (His or H), **isoleucine (Ile or I), leucine (Leu or**

	L), lysine (Lys or K), methionine (Met or M), **proline (Pro or P)**, phenylalanine (Phe or F), **serine (Ser or S)**, **tryptophan (Trp or W)**, **threonine (Thr or T)**, **tyrosine (Tyr or Y)**, and **valine (Val or V)**. In a preferred embodiment, the peptide comprises only naturally occurring amino acids and/or only L-amino acids. Each amino acid can be an unnatural, non-standard, or synthetic amino acids, such as aminohexanoic acid, biphenylalanine, cyclohexylalanine, cyclohexylglycine, diethylglycine, dipropylglycine, 2,3-diaminoproprionic acid, homophenylalanine, homoserine, homotyrosine, naphthylalanine, norleucine, ornithine, phenylalanine (4-fluoro), phenylalanine(2,3,4,5,6-pentafluoro), phenylalanine(4-nitro), phenylglycine, **pipecolic acid**, sarcosine, tetrahydroisoquinoline-3-carboxylic acid, and **tert-leucine**. Preferably, synthetic amino acids with alkyl side chains are selected from C1-C17 alkyls, preferably C1-C6 alkyls. In one embodiment, the peptide comprises one or more amino acid alcohols, e.g., serine and threonine. In another embodiment, the peptide comprises one or more N-methyl amino acids, e.g., N-methyl aspartic acid." 3. MAZUR (1970) "Structure-taste relation of aspartic acid amides" J. Med. Chem. Vol 13(6): 1217-1221.

Table 2 (entry 64):

TABLE II

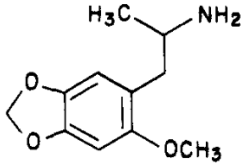
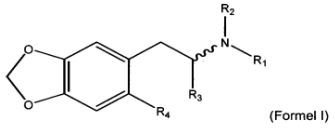
ASPARTIC ACID AMIDES
Asp-X[a]

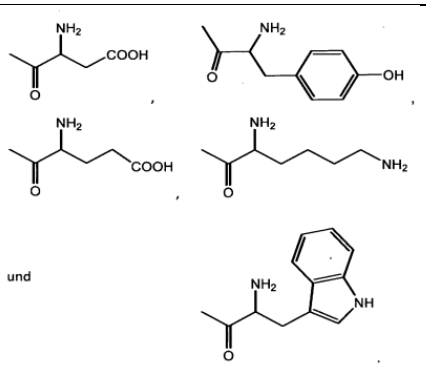
No.	X	Yield,[b] %	Mp, °C	[α]D, deg	Formula[c]	Taste
50	HNCH(CH3)CH2C6H5; L-	88 AC	197–198 W	−12 M	C13H18N2O3	50
51	HNCH(CH3)CH2C6H5; D-	98 AC	222–225 E W	+14 W	C13H18N2O3	0
52	HNCH(CH3)CH2C6H5[d]	79 M	164–166 A-W	+34 M	C13H18N2O3	-
53	HNCH2CH2C6H5	70 AC	212–214 P-W	−15 W	C12H16N2O3	0
54	HNCH(C2H5)CH2C6H5	91 AC	158–163 M-ET	+8 M	C14H20N2O3·0.25H2O	5
55	HNC(CH3)2CH2C6H5	96 AC	159–161 W	−16 M	C14H20N2O3	20
56		91 M	223–224 M-W	−6 H	C13H16N2O3	10
57	HNCHCHC6H5; L-	95 M	175–178	+5 M	C13H16N2O3·H2O	-
58	HNCH2CH(CH3)C6H5	70 AC	182–188 W	−20 W	C12H18N2O3	-
59	N(CH3)CH(CH3)CH2C6H5; L-	84 M	164–166	+47 W	C14H20N2O3·0.5H2O	-
60	N(CH3)CH(CH3)CH2C6H5; D-	82 M	185–187	+12 W	C14H20N2O3·0.5H2O	-
61	HNCH(CH3)CH2CH2C6H5	95 AC	190–196 M-W	+16 H	C13H18N2O3	5
62	HNCH(CH3)CH2OC6H5	68 M	180–184 M-W	+11 H	C12H16N2O3	10
63	HNCH2CH2OC6H5	85 AC	184–185 W	−13 H	C11H14N2O3	+
64	HNCH(CH3)CH2C6H3(OCH2O)-3,4	95 M	189–192	+6 M	C13H16N2O5	-
65	HNCH(CH2OH)CH2C6H5; L-	95 AC	237–238 W	−26 AC	C13H18N2O3	+
66	HNCH(CH3)CH(OH)C6H5	98 M	188–190 M	+10 M	C13H18N2O3·0.5H2O	+
67	HNCH(CH3)CH2C6H4OH-4	95 M	160–185	+5 W	C13H18N2O3	+
68	HNCH2CH2C6H4OH-4	72 AC	209–210 W	−21 W	C12H16N2O3	+
69	HNCH(CH2OH)CH2C6H4OH-4; L-	44 M	212–213 M	−10 H	C13H18N2O3	+
70	HNCH(CH3)CH2C6H4NHSO2CH3-4; L-	96 M	199–208 W	+14 H	C13H19N3O4S	-
71	HNCH(CH3)CH2C6H4F-4	87 M	203–209 M-ET	+9 H	C13H17FN2O3	20
72	HNCH2CH2C6H4F-4	74 M	208–209 W	−6 M	C12H15FN2O3	5
73		85 M	168–180 M-ET	+6 H	C11H16N2O3·0.333H2O	10
74		71 M	195–196 M	−17 M	C10H14N2O3	+
75		96 AC	203–205 M	−22 M	C15H19N3O3	-
76	HNCH(CH3)CH2-c-C6H11; L-	84 AC	184–185 M-W	−19 M	C13H24N2O3	50
77	HNCH(CH3)CH2-c-C6H11; D-	60 M	207–208 M-W	+16 M	C13H24N2O3	5
78	HNCH2CH2-c-C6H11	94 AC	193–202 M-W	+7 AC	C12H22N2O3	10
79	N(CH3)CH(CH3)CH2-c-C6H11; L-	78 M	179–180 P-ET	−14 W	C14H26N2O3·0.25H2O	-
80	N(CH3)CH(CH3)CH2-c-C6H11; D-	64 M	194–196	+1 W	C14H26N2O3	-
81	HN-c-C6H11	91 M	224–227 W	+16 H	C10H18N2O3	-
82	HNCH(CH3)CH2CH2CH3	92 M	190–194 A-W	+9 AC	C7H14N2O3·0.5H2O	0
83	HN(CH2)3CH(CH3)CH3	89 M	222–223 M-W		C10H20N2O3	0
84	HNCH(CH3)CH2CH(CH3)CH3; L-	91 AC	168–168 W	−17 M	C10H20N2O3·0.5H2O	-
85	HNCH(CH3)CH2CH(CH3)CH3; D-	92 AC	201–202 W	+9 M	C10H20N2O3·0.25H2O	-
86	HNCH(C2H5)CH2CH2CH3	93 M	196–200 A-W	+12 AC	C10H20N2O3·H2O	-
87	HN(CH2)3CH3	88 M	200–201 W	+9 AC	C10H20N2O3·0.25H2O	+
88	HNCH(CH3)(CH2)3CH3	98 M	188–193 A-W	+11 AC	C10H20N2O3·0.5H2O	30
89	HN(CH2)4CH3	89 M	200–201 W	+8 AC	C11H22N2O3·0.25H2O	+
90	HNCH(CH3)(CH2)4CH3	95 M	190–194	+7 AC	C11H22N2O3	20
91	HNCH(CH3)CH2CH(CH3)CH2CH3	94 M	162–166 W	−2 M	C11H22N2O3·0.25H2O	+
92	HNCH(CH3)CH2CH2CH(CH3)CH3	94 M	183–188 A-W	+9 AC	C11H22N2O3·0.25H2O	50
93	HNCH(C2H5)(CH2)2CH3	98 M	190–195	+9 AC	C11H22N2O3·0.5H2O	+
94	HNCH(CH3)(CH2)4CH3; L-	94 M	187–189 W	−5 M	C11H22N2O3·H2O	50
95	HNCH(CH3)(CH2)4CH3; L[d]	97 M	213–214 M-W	−5 M	C11H22N2O3·0.5H2O	-
96	HNCH(CH3)(CH2)4CH3; D-	96 M	217–218 M-W	+5 M	C11H22N2O3	0
97	HNCH(CH3)(CH2)4CH3; D[d]	97 M	189–192 W	+6 M	C11H22N2O3	-
98	HNCH(CH3)CH2CH2CH(CH3)CH3; L-	84 M	187–190 W	+23 H	C11H22N2O3·0.5H2O	100
99	HNCH(CH3)CH2CH2CH(CH3)CH3; L[d]	90 M	215–216 M-W	+2 M	C11H22N2O3	0
100	HNCH(CH3)CH2CH2CH(CH3)CH3; D-	96 M	210–213 M-W	−3 M	C11H22N2O3·0.5H2O	+
101	HNCH(CH3)CH2CH2CH(CH3)CH3; D[d]	91 M	192–195 W	−26 H	C11H22N2O3·0.25H2O	-
102	HNCH(CH3)CH2CH2OCH2CH3	77 M	166–170 M-ET	+3 M	C10H20N2O4·0.25H2O	10
103	HNCH(CH3)(CH2)5CH3	85 M	180–190	−8 M	C12H24N2O3·0.5H2O	10

[a] See Table I for abbreviations and explanations. [b] The amide was derived from L-Glu. [c] The amide was derived from DL-Asp. [d] The amide was derived from D-Asp. [e] All compounds were analyzed for C, H, N.

4. Gatch (2016) “Locomotor, discriminative stimulus, and place conditioning effects of MDAI in rodents” Behavioral Pharmacology, Vol 27 (6): 497-505.

From **abstract**: “5,6-Methylenedioxy-2-aminoindane (MDAI) has become a common substitute for (±)-3,4-methylenedioxymethamphetamine (MDMA) in Ecstasy. **MDAI is known to produce MDMA-like discriminative stimulus effects**, but it is not known whether MDAI has psychostimulant or hallucinogen-like effects. MDAI was tested for locomotor stimulant effects in mice and subsequently for discriminative stimulus effects in rats trained to discriminate cocaine (10 mg/kg, intraperitoneally), methamphetamine (1 mg/kg, intraperitoneally), ±MDMA (1.5 mg/kg, intraperitoneally), or (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride

	(0.5 mg/kg, intraperitoneally) from saline…MDAI fully substituted for the discriminative stimulus effects of MDMA (2.5 mg/kg), (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride (5 mg/kg), and cocaine (7.5 mg/kg), but produced only 73% methamphetamine-appropriate responding at a dose that suppressed responding (7.5 mg/kg). MDAI produced tremors at 10 mg/kg in one methamphetamine-trained rat. MDAI produced conditioned place preference from 0.3 to 10 mg/kg. **The effects of MDAI on locomotor activity and drug discrimination were similar to those produced by MDMA, having both psychostimulant-like and hallucinogen-like effects**; thus, MDAI may have similar abuse potential as MDMA. 5. Nichols (1986) "Synthesis and Evaluation of 2,3-Dihydrobenzofuran Analogues of the Hallucinogen 1-(2,5-Dimethoxy-4methylphenyl)-2-aminopropane: Drug Discrimination Studies in Rats" Vol. 29 (2): 302-304. From **page 304, paragraph 2**: "This is all the more difficult to explain in light of the fact that 2-methoxy-4,5-(methylenedioxy)amphetamine (8; MMDA-2) is active  8 and produces clear central effects at an oral dosage of 25 mg of the hydrochloride"
9. A pharmaceutical composition comprising at least one compound of claim 1 and one or more pharmaceutically acceptable excipients.	*From the application of interest's priority document DE 10 2020 123 793.6 (filed 11 September 2020):* From **claim 1**: "1. 3,4-methylenedioxy-amphetamine peptide according to general formula I:  (Formel I) where R1 is selected from the group consisting of:



where R2 is selected from the group consisting of:
-H or -CH3.
where R3 is selected from the group consisting of:
-CH3 or -CH2-R4
where R4 is selected from the group consisting of:
-H, -OCH3, or R3-CH2-

1. US Priority Doc. No. 63/115,245 of US Pat. Doc. No. 17/518,846 "MDMA PRODRUGS TO ASSIST PSYCHOTHERAPY" (Priority doc filed 18 November 2020).

From **claim 1**: "A compound comprising a prodrug including a psychoactive base substance attached to an amino acid."

From **claim 3**: "The compound of claim 2, wherein the MDMA or MDMA-like substance is chosen from the group consisting of MDA…MDAI…mixed dopaminergic-serotonergic amphetamine and their N-alkylated analogs..."

From **claim 4**: "The compound of claim 1, wherein said amino acid is chosen from the group consisting of lysine, alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine."

From **claim 5**: "The compound of claim 1, wherein the amino acid is chosen from the group consisting of natural or synthetic."

Figure 1A:

Fig. 1A

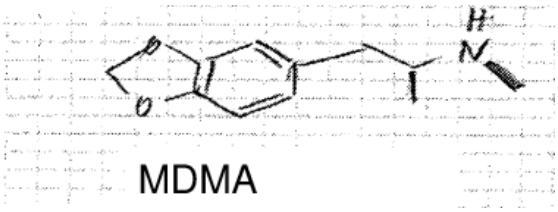
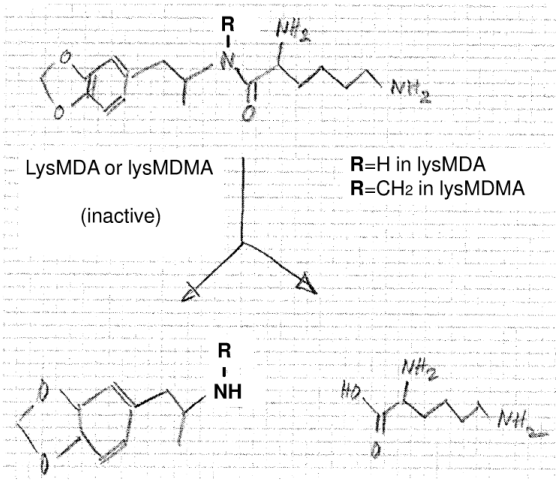


Figure 2:

Fig. 2



2. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009).

From **claim 1**: "A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt thereof, said method comprising orally administering to said subject a prodrug or a salt thereof said **prodrug comprising said amphetamine covalently bonded to a single amino acid** or to a peptide comprising from 2 to 10 amino acids, whereby the blood levels of said amphetamine achieve a therapeutically effect level but said blood levels do not result in a euphoric effect."

From **paragraph [0096]**: "**The amphetamine, A, can be any of the sympathomimetic phenethylamine derivatives which have central nervous system stimulant activity** such as amphetamine, or any derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, **methylenedioxyamphetamine**, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-

	trimethoxyamphetamine, and **3,4-methylenedioxymethamphetamine**…" From **paragraph [0107]**: "Each amino acid can be any one of the L- or D-enantiomers, preferably L-enantiomers, of the naturally occurring amino acids: **alanine (Ala or A)**, arginine (Arg or R), **asparagine (Asn or N)**, aspartic acid (Asp or D), cysteine (Cys or C), glycine (Gly or G), **glutamic acid (Glu or E)**, **glutamine (Gln or Q)**, histidine (His or H), **isoleucine (Ile or I), leucine (Leu or L),** lysine (Lys or K), methionine (Met or M), **proline (Pro or P)**, phenylalanine (Phe or F), **serine (Ser or S)**, **tryptophan (Trp or W)**, **threonine (Thr or T)**, **tyrosine (Tyr or Y)**, and **valine (Val or V)**. In a preferred embodiment, the peptide comprises only naturally occurring amino acids and/or only L-amino acids. Each amino acid can be an unnatural, non-standard, or synthetic amino acids, such as aminohexanoic acid, biphenylalanine, cyclohexylalanine, cyclohexylglycine, diethylglycine, dipropylglycine, 2,3-diaminoproprionic acid, homophenylalanine, homoserine, homotyrosine, naphthylalanine, norleucine, ornithine, phenylalanine (4-fluoro), phenylalanine(2,3,4,5,6-pentafluoro), phenylalanine(4-nitro), phenylglycine, **pipecolic acid**, sarcosine, tetrahydroisoquinoline-3-carboxylic acid, and **tert-leucine**. Preferably, synthetic amino acids with alkyl side chains are selected from C1-C17 alkyls, preferably C1-C6 alkyls. In one embodiment, the peptide comprises one or more amino acid alcohols, e.g., serine and threonine. In another embodiment, the peptide comprises one or more N-methyl amino acids, e.g., N-methyl aspartic acid." 3. MAZUR (1970) "Structure-taste relation of aspartic acid amides" J. Med. Chem. Vol 13(6): 1217-1221.

Table 2 (entry 64):

TABLE II

ASPARTIC ACID AMIDES
Asp-X[a]

No.	X	Yield,[b] %	Mp, °C	[α]D, deg	Formula[c]	Taste
50	HNCH(CH3)CH2C6H5; L-	88 AC	197–198 W	−12 M	C13H18N2O3	50
51	HNCH(CH3)CH2C6H5; D-	98 AC	222–225 E W	+14 W	C13H18N2O3	0
52	HNCH(CH3)CH2C6H5[d]	79 M	164–166 A-W	+34 M	C13H18N2O3	-
53	HNCH2CH2C6H5	70 AC	212–214 P-W	−15 W	C12H16N2O3	0
54	HNCH(C2H5)CH2C6H5	91 AC	158–163 M-ET	+8 M	C14H20N2O3·0.25H2O	5
55	HNC(CH3)2CH2C6H5	96 AC	159–161 W	−16 M	C14H20N2O3	20
56		91 M	223–224 M-W	−6 H	C13H16N2O3	10
57	HNCHCHC6H5; L-	95 M	175–178	+5 M	C13H16N2O3·H2O	-
58	HNCH2CH(CH3)C6H5	70 AC	182–188 W	−20 W	C12H18N2O3	-
59	N(CH3)CH(CH3)CH2C6H5; L-	84 M	164–166	+47 W	C14H20N2O3·0.5H2O	-
60	N(CH3)CH(CH3)CH2C6H5; D-	82 M	185–187	+12 W	C14H20N2O3·0.5H2O	-
61	HNCH(CH3)CH2CH2C6H5	95 AC	190–196 M-W	+16 H	C13H18N2O3	5
62	HNCH(CH3)CH2OC6H5	68 M	180–184 M-W	+11 H	C12H16N2O3	10
63	HNCH2CH2OC6H5	85 AC	184–185 W	−13 H	C11H14N2O3	+
64	HNCH(CH3)CH2C6H3(OCH2O)-3,4	95 M	189–192	+6 M	C13H16N2O5	-
65	HNCH(CH2OH)CH2C6H5; L-	95 AC	237–238 W	−26 AC	C13H18N2O3	+
66	HNCH(CH3)CH(OH)C6H5	98 M	188–190 M	+10 M	C13H18N2O3·0.5H2O	+
67	HNCH(CH3)CH2C6H4OH-4	95 M	160–185	+5 W	C13H18N2O3	+
68	HNCH2CH2C6H4OH-4	72 AC	209–210 W	−21 W	C12H16N2O3	+
69	HNCH(CH2OH)CH2C6H4OH-4; L-	44 M	212–213 M	−10 H	C13H18N2O3	+
70	HNCH(CH3)CH2C6H4NHSO2CH3-4; L-	96 M	199–208 W	+14 H	C13H19N3O4S	-
71	HNCH(CH3)CH2C6H4F-4	87 M	203–209 M-ET	+9 H	C13H17FN2O3	20
72	HNCH2CH2C6H4F-4	74 M	208–209 W	−6 M	C12H15FN2O3	5
73		85 M	168–180 M-ET	+6 H	C11H16N2O3·0.333H2O	10
74		71 M	195–196 M	−17 M	C10H14N2O3	+
75		96 AC	203–205 M	−22 M	C15H19N3O3	-
76	HNCH(CH3)CH2-c-C6H11; L-	84 AC	184–185 M-W	−19 M	C13H24N2O3	50
77	HNCH(CH3)CH2-c-C6H11; D-	60 M	207–208 M-W	+16 M	C13H24N2O3	5
78	HNCH2CH2-c-C6H11	94 AC	193–202 M-W	+7 AC	C12H22N2O3	10
79	N(CH3)CH(CH3)CH2-c-C6H11; L-	78 M	179–180 P-ET	−14 W	C14H26N2O3·0.25H2O	-
80	N(CH3)CH(CH3)CH2-c-C6H11; D-	64 M	194–196	+1 W	C14H26N2O3	-
81	HN-c-C6H11	91 M	224–227 W	+16 H	C10H18N2O3	-
82	HNCH(CH3)CH2CH2CH3	92 M	190–194 A-W	+9 AC	C7H14N2O3·0.5H2O	0
83	HN(CH2)3CH(CH3)CH3	89 M	222–223 M-W		C10H20N2O3	0
84	HNCH(CH3)CH2CH(CH3)CH3; L-	91 AC	168–168 W	−17 M	C10H20N2O3·0.5H2O	-
85	HNCH(CH3)CH2CH(CH3)CH3; D-	92 AC	201–202 W	+9 M	C10H20N2O3·0.25H2O	-
86	HNCH(C2H5)CH2CH2CH3	93 M	196–200 A-W	+12 AC	C10H20N2O3·H2O	-
87	HN(CH2)3CH3	88 M	200–201 W	+9 AC	C10H20N2O3·0.25H2O	+
88	HNCH(CH3)(CH2)3CH3	98 M	188–193 A-W	+11 AC	C10H20N2O3·0.5H2O	30
89	HN(CH2)4CH3	89 M	200–201 W	+8 AC	C11H22N2O3·0.25H2O	+
90	HNCH(CH3)(CH2)4CH3	95 M	190–194	+7 AC	C11H22N2O3	20
91	HNCH(CH3)CH2CH(CH3)CH2CH3	94 M	162–166 W	−2 M	C11H22N2O3·0.25H2O	+
92	HNCH(CH3)CH2CH2CH(CH3)CH3	94 M	183–188 A-W	+9 AC	C11H22N2O3·0.25H2O	50
93	HNCH(C2H5)(CH2)2CH3	98 M	190–195	+9 AC	C11H22N2O3·0.5H2O	+
94	HNCH(CH3)(CH2)4CH3; L-	94 M	187–189 W	−5 M	C11H22N2O3·H2O	50
95	HNCH(CH3)(CH2)4CH3; L[d]	97 M	213–214 M-W	−5 M	C11H22N2O3·0.5H2O	-
96	HNCH(CH3)(CH2)4CH3; D-	96 M	217–218 M-W	+5 M	C11H22N2O3	0
97	HNCH(CH3)(CH2)4CH3; D[d]	97 M	189–192 W	+6 M	C11H22N2O3	-
98	HNCH(CH3)CH2CH2CH(CH3)CH3; L-	84 M	187–190 W	+23 H	C11H22N2O3·0.5H2O	100
99	HNCH(CH3)CH2CH2CH(CH3)CH3; L[d]	90 M	215–216 M-W	+2 M	C11H22N2O3	0
100	HNCH(CH3)CH2CH2CH(CH3)CH3; D-	96 M	210–213 M-W	−3 M	C11H22N2O3·0.5H2O	+
101	HNCH(CH3)CH2CH2CH(CH3)CH3; D[d]	91 M	192–195 W	−26 H	C11H22N2O3·0.25H2O	-
102	HNCH(CH3)CH2CH2OCH2CH3	77 M	166–170 M-ET	+3 M	C10H20N2O4·0.25H2O	10
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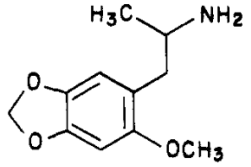
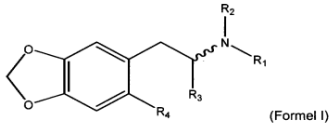
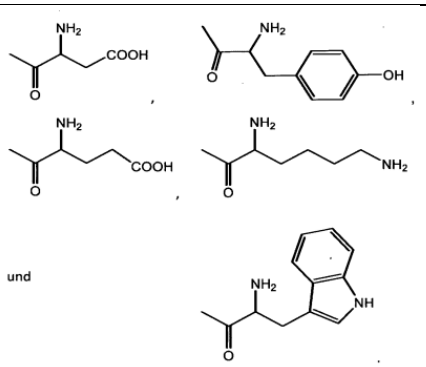
[a] See Table I for abbreviations and explanations. [b] The amide was derived from L-Glu. [c] The amide was derived from DL-Asp. [d] The amide was derived from D-Asp. [e] All compounds were analyzed for C, H, N.

4. Gatch (2016) “Locomotor, discriminative stimulus, and place conditioning effects of MDAI in rodents” Behavioral Pharmacology, Vol 27 (6): 497-505.

From **abstract**: “5,6-Methylenedioxy-2-aminoindane (MDAI) has become a common substitute for (±)-3,4-methylenedioxymethamphetamine (MDMA) in Ecstasy. **MDAI is known to produce MDMA-like discriminative stimulus effects**, but it is not known whether MDAI has psychostimulant or hallucinogen-like effects. MDAI was tested for locomotor stimulant effects in mice and subsequently for discriminative stimulus effects in rats trained to discriminate cocaine (10 mg/kg, intraperitoneally), methamphetamine (1 mg/kg, intraperitoneally), ±MDMA (1.5 mg/kg, intraperitoneally), or (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride

	(0.5 mg/kg, intraperitoneally) from saline…MDAI fully substituted for the discriminative stimulus effects of MDMA (2.5 mg/kg), (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride (5 mg/kg), and cocaine (7.5 mg/kg), but produced only 73% methamphetamine-appropriate responding at a dose that suppressed responding (7.5 mg/kg). MDAI produced tremors at 10 mg/kg in one methamphetamine-trained rat. MDAI produced conditioned place preference from 0.3 to 10 mg/kg. **The effects of MDAI on locomotor activity and drug discrimination were similar to those produced by MDMA, having both psychostimulant-like and hallucinogen-like effects**; thus, MDAI may have similar abuse potential as MDMA. 5. Nichols (1986) "Synthesis and Evaluation of 2,3-Dihydrobenzofuran Analogues of the Hallucinogen 1-(2,5-Dimethoxy-4methylphenyl)-2-aminopropane: Drug Discrimination Studies in Rats" Vol. 29 (2): 302-304. From **page 304, paragraph 2**: "This is all the more difficult to explain in light of the fact that 2-methoxy-4,5-(methylenedioxy)amphetamine (8; MMDA-2) is active  8 and produces clear central effects at an oral dosage of 25 mg of the hydrochloride"
14. A method of treating a serotonin 5-HT_{2A} receptor associated disease/disorder in a subject in need thereof, the method comprising administering a therapeutically effective amount of the compound of claim 1 to said subject.	*From the application of interest's priority document DE 10 2020 123 793.6 (filed 11 September 2020):* From **claim 1**: "1. 3,4-methylenedioxy-amphetamine peptide according to general formula I:  (Formel I) where R1 is selected from the group consisting of:



where R2 is selected from the group consisting of:
-H or -CH3.
where R3 is selected from the group consisting of:
-CH3 or -CH2-R4
where R4 is selected from the group consisting of:
-H, -OCH3, or R3-CH2-

1. US Priority Doc. No. 63/115,245 of US Pat. Doc. No. 17/518,846 "MDMA PRODRUGS TO ASSIST PSYCHOTHERAPY" (Priority doc filed 18 November 2020).

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From **claim 3**: "The compound of claim 2, wherein the MDMA or MDMA-like substance is chosen from the group consisting of MDA…MDAI…mixed dopaminergic-serotonergic amphetamine and their N-alkylated analogs..."

From **claim 4**: "The compound of claim 1, wherein said amino acid is chosen from the group consisting of lysine, alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine."

From **claim 5**: "The compound of claim 1, wherein the amino acid is chosen from the group consisting of natural or synthetic."

Figure 1A:

Fig. 1A

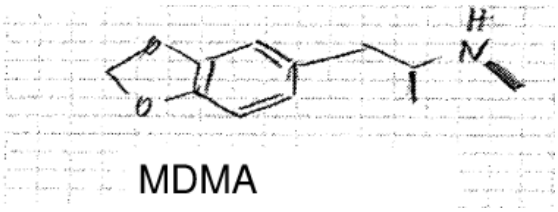
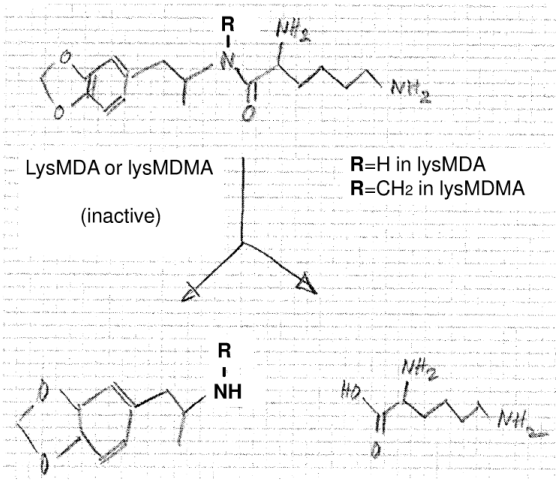


Figure 2:

Fig. 2



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From **paragraph [0096]**: "**The amphetamine, A, can be any of the sympathomimetic phenethylamine derivatives which have central nervous system stimulant activity** such as amphetamine, or any derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, **methylenedioxyamphetamine**, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-

	trimethoxyamphetamine, and **3,4-methylenedioxymethamphetamine**…" From **paragraph [0107]**: "Each amino acid can be any one of the L- or D-enantiomers, preferably L-enantiomers, of the naturally occurring amino acids: alanine (Ala or A), arginine (Arg or R), asparagine (Asn or N), **aspartic acid (Asp or D)**, cysteine (Cys or C), glycine (Gly or G), **glutamic acid (Glu or E**), glutamine (Gln or Q), histidine (His or H), isoleucine (Ile or I), leucine (Leu or L), **lysine (Lys or K)**, methionine (Met or M), proline (Pro or P), phenylalanine (Phe or F), serine (Ser or S), **tryptophan (Trp or W)**, threonine (Thr or T), **tyrosine (Tyr or Y)**, and valine (Val or V)…" 3. MAZUR (1970) "Structure-taste relation of aspartic acid amides" J. Med. Chem. Vol 13(6): 1217-1221.

Table 2 (entry 64):

TABLE II

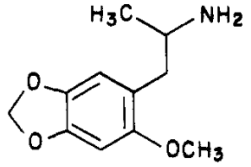
ASPARTIC ACID AMIDES
Asp-X[a]

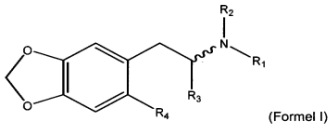
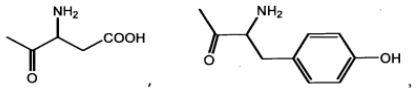
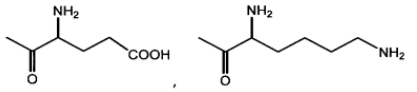
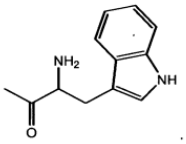
No.	X	Yield,[b] %	Mp, °C	[α]D, deg	Formula[c]	Taste
50	HNCH(CH3)CH2C6H5; L-	88 AC	197–198 W	−12 M	C13H18N2O3	50
51	HNCH(CH3)CH2C6H5; D-	98 AC	222–225 E W	+14 W	C13H18N2O3	0
52	HNCH(CH3)CH2C6H5[d]	79 M	164–166 A-W	+34 M	C13H18N2O3	-
53	HNCH2CH2C6H5	70 AC	212–214 P-W	−15 W	C12H16N2O3	0
54	HNCH(C2H5)CH2C6H5	91 AC	158–163 M-ET	+8 M	C14H20N2O3·0.25H2O	5
55	HNC(CH3)2CH2C6H5	96 AC	159–161 W	−16 M	C14H20N2O3	20
56		91 M	223–224 M-W	−6 H	C13H16N2O3	10
57	HNCHCHC6H5; L-	95 M	175–178	+5 M	C13H16N2O3·H2O	-
58	HNCH2CH(CH3)C6H5	70 AC	182–188 W	−20 W	C12H18N2O3	-
59	N(CH3)CH(CH3)CH2C6H5; L-	84 M	164–166	+47 W	C14H20N2O3·0.5H2O	-
60	N(CH3)CH(CH3)CH2C6H5; D-	82 M	185–187	+12 W	C14H20N2O3·0.5H2O	-
61	HNCH(CH3)CH2CH2C6H5	95 AC	190–196 M-W	+16 H	C13H18N2O3	5
62	HNCH(CH3)CH2OC6H5	68 M	180–184 M-W	+11 H	C12H16N2O3	10
63	HNCH2CH2OC6H5	85 AC	184–185 W	−13 H	C11H14N2O3	+
64	HNCH(CH3)CH2C6H3(OCH2O)-3,4	95 M	189–192	+6 M	C13H16N2O5	-
65	HNCH(CH2OH)CH2C6H5; L-	95 AC	237–238 W	−26 AC	C13H18N2O3	+
66	HNCH(CH3)CH(OH)C6H5	98 M	188–190 M	+10 M	C13H18N2O3·0.5H2O	+
67	HNCH(CH3)CH2C6H4OH-4	95 M	160–185	+5 W	C13H18N2O3	+
68	HNCH2CH2C6H4OH-4	72 AC	209–210 W	−21 W	C12H16N2O3	+
69	HNCH(CH2OH)CH2C6H4OH-4; L-	44 M	212–213 M	−10 H	C13H18N2O3	+
70	HNCH(CH3)CH2C6H4NHSO2CH3-4; L-	96 M	199–208 W	+14 H	C13H19N3O4S	-
71	HNCH(CH3)CH2C6H4F-4	87 M	203–209 M-ET	+9 H	C13H17FN2O3	20
72	HNCH2CH2C6H4F-4	74 M	208–209 W	−6 M	C12H15FN2O3	5
73		85 M	168–180 M-ET	+6 H	C11H16N2O3·0.333H2O	10
74		71 M	195–196 M	−17 M	C10H14N2O3	+
75		96 AC	203–205 M	−22 M	C15H19N3O3	-
76	HNCH(CH3)CH2-c-C6H11; L-	84 AC	184–185 M-W	−19 M	C13H24N2O3	50
77	HNCH(CH3)CH2-c-C6H11; D-	60 M	207–208 M-W	+16 M	C13H24N2O3	5
78	HNCH2CH2-c-C6H11	94 AC	193–202 M-W	+7 AC	C12H22N2O3	10
79	N(CH3)CH(CH3)CH2-c-C6H11; L-	78 M	179–180 P-ET	−14 W	C14H26N2O3·0.25H2O	-
80	N(CH3)CH(CH3)CH2-c-C6H11; D-	64 M	194–196	+1 W	C14H26N2O3	-
81	HN-c-C6H11	91 M	224–227 W	+16 H	C10H18N2O3	-
82	HNCH(CH3)CH2CH2CH3	92 M	190–194 A-W	+9 AC	C7H14N2O3·0.5H2O	0
83	HN(CH2)3CH(CH3)CH3	89 M	222–223 M-W		C10H20N2O3	0
84	HNCH(CH3)CH2CH(CH3)CH3; L-	91 AC	168–168 W	−17 M	C10H20N2O3·0.5H2O	-
85	HNCH(CH3)CH2CH(CH3)CH3; D-	92 AC	201–202 W	+9 M	C10H20N2O3·0.25H2O	-
86	HNCH(C2H5)CH2CH2CH3	93 M	196–200 A-W	+12 AC	C10H20N2O3·H2O	-
87	HN(CH2)3CH3	88 M	200–201 W	+9 AC	C10H20N2O3·0.25H2O	+
88	HNCH(CH3)(CH2)3CH3	98 M	188–193 A-W	+11 AC	C10H20N2O3·0.5H2O	30
89	HN(CH2)4CH3	89 M	200–201 W	+8 AC	C11H22N2O3·0.25H2O	+
90	HNCH(CH3)(CH2)4CH3	95 M	190–194	+7 AC	C11H22N2O3	20
91	HNCH(CH3)CH2CH(CH3)CH2CH3	94 M	162–166 W	−2 M	C11H22N2O3·0.25H2O	+
92	HNCH(CH3)CH2CH2CH(CH3)CH3	94 M	183–188 A-W	+9 AC	C11H22N2O3·0.25H2O	50
93	HNCH(C2H5)(CH2)2CH3	98 M	190–195	+9 AC	C11H22N2O3·0.5H2O	+
94	HNCH(CH3)(CH2)4CH3; L-	94 M	187–189 W	−5 M	C11H22N2O3·H2O	50
95	HNCH(CH3)(CH2)4CH3; L[d]	97 M	213–214 M-W	−5 M	C11H22N2O3·0.5H2O	-
96	HNCH(CH3)(CH2)4CH3; D-	96 M	217–218 M-W	+5 M	C11H22N2O3	0
97	HNCH(CH3)(CH2)4CH3; D[d]	97 M	189–192 W	+6 M	C11H22N2O3	-
98	HNCH(CH3)CH2CH2CH(CH3)CH3; L-	84 M	187–190 W	+23 H	C11H22N2O3·0.5H2O	100
99	HNCH(CH3)CH2CH2CH(CH3)CH3; L[d]	90 M	215–216 M-W	+2 M	C11H22N2O3	0
100	HNCH(CH3)CH2CH2CH(CH3)CH3; D-	96 M	210–213 M-W	−3 M	C11H22N2O3·0.5H2O	+
101	HNCH(CH3)CH2CH2CH(CH3)CH3; D[d]	91 M	192–195 W	−26 H	C11H22N2O3·0.25H2O	-
102	HNCH(CH3)CH2CH2OCH2CH3	77 M	166–170 M-ET	+3 M	C10H20N2O4·0.25H2O	10
103	HNCH(CH3)(CH2)5CH3	85 M	180–190	−8 M	C12H24N2O3·0.5H2O	10

[a] See Table I for abbreviations and explanations. [b] The amide was derived from L-Glu. [c] The amide was derived from DL-Asp. [d] The amide was derived from D-Asp. [e] All compounds were analyzed for C, H, N.

4. Gatch (2016) “Locomotor, discriminative stimulus, and place conditioning effects of MDAI in rodents” Behavioral Pharmacology, Vol 27 (6): 497-505.

From **abstract**: “5,6-Methylenedioxy-2-aminoindane (MDAI) has become a common substitute for (±)-3,4-methylenedioxymethamphetamine (MDMA) in Ecstasy. **MDAI is known to produce MDMA-like discriminative stimulus effects**, but it is not known whether MDAI has psychostimulant or hallucinogen-like effects. MDAI was tested for locomotor stimulant effects in mice and subsequently for discriminative stimulus effects in rats trained to discriminate cocaine (10 mg/kg, intraperitoneally), methamphetamine (1 mg/kg, intraperitoneally), ±MDMA (1.5 mg/kg, intraperitoneally), or (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride

	(0.5 mg/kg, intraperitoneally) from saline…MDAI fully substituted for the discriminative stimulus effects of MDMA (2.5 mg/kg), (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride (5 mg/kg), and cocaine (7.5 mg/kg), but produced only 73% methamphetamine-appropriate responding at a dose that suppressed responding (7.5 mg/kg). MDAI produced tremors at 10 mg/kg in one methamphetamine-trained rat. MDAI produced conditioned place preference from 0.3 to 10 mg/kg. **The effects of MDAI on locomotor activity and drug discrimination were similar to those produced by MDMA, having both psychostimulant-like and hallucinogen-like effects**; thus, MDAI may have similar abuse potential as MDMA. 5. Nichols (1986) "Synthesis and Evaluation of 2,3-Dihydrobenzofuran Analogues of the Hallucinogen 1-(2,5-Dimethoxy-4methylphenyl)-2-aminopropane: Drug Discrimination Studies in Rats" Vol. 29 (2): 302-304. From **page 304, paragraph 2**: "This is all the more difficult to explain in light of the fact that 2-methoxy-4,5-(methylenedioxy)amphetamine (8; MMDA-2) is active  8 and produces clear central effects at an oral dosage of 25 mg of the hydrochloride" 6. Bahji (2019) "Efficacy of 3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy for posttraumatic stress disorder: A systematic review and meta-analysis" Progress in Neuropsychopharmacology &Biological Psychiatry, Vol. 96, 109735. From **page 8, conclusions**: "We systematically reviewed and meta-analyzed randomized and quasi-randomized controlled trials measuring the effectiveness and safety MDMA-assisted psychotherapy for treating chronic, treatment-refractory PTSD. We identified five moderate-quality trials demonstrating that MDMA-assisted psychotherapy was associated with significant improvements in PTSD symptoms following intervention that extended long-term with few reported adverse effects. **Taken together, our synthesis suggests that MDMA-assisted psychotherapy is a potentially safe, effective,**

	and durable treatment for individuals with treatment-refractory PTSD."
15. The method of claim 14, wherein said disease/disorder is an anxiety disorder, attention deficit hyperactivity disorder (ADHD), posttraumatic stress disorder (PTSD), depression, cluster headache, ca condition associated with cancer, diminished drive, burn-out, bore-out, migraine, Parkinson's disease, pulmonary hypertension, schizophrenia, an eating disorder, nausea, or vomiting.	*From the application of interest's priority document DE 10 2020 123 793.6 (filed 11 September 2020):* From **claim 1**: "1. 3,4-methylenedioxy-amphetamine peptide according to general formula I:  (Formel I) where R1 is selected from the group consisting of:   und  where R2 is selected from the group consisting of: -H or -CH3. where R3 is selected from the group consisting of: -CH3 or -CH2-R4 where R4 is selected from the group consisting of: -H, -OCH3, or R3-CH2- 1. US Priority Doc. No. 63/115,245 of US Pat. Doc. No. 17/518,846 "MDMA PRODRUGS TO ASSIST PSYCHOTHERAPY" (Priority doc filed 18 November 2020). From **claim 1**: "A compound comprising a prodrug including a psychoactive base substance attached to an amino acid." From **claim 3**: "The compound of claim 2, wherein the MDMA or MDMA-like substance is chosen from the group consisting of MDA…MDAI…mixed dopaminergic-serotonergic amphetamine and their N-alkylated analogs..." From **claim 4**: "The compound of claim 1, wherein said amino acid is chosen from the group consisting of lysine, alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine,

leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine."

From **claim 5**: "The compound of claim 1, wherein the amino acid is chosen from the group consisting of natural or synthetic."

Figure 1A:

Fig. 1A

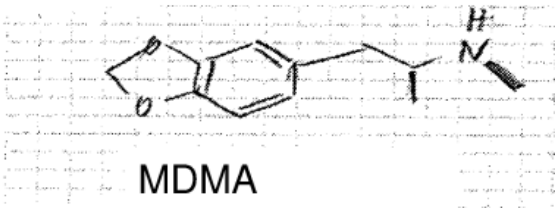
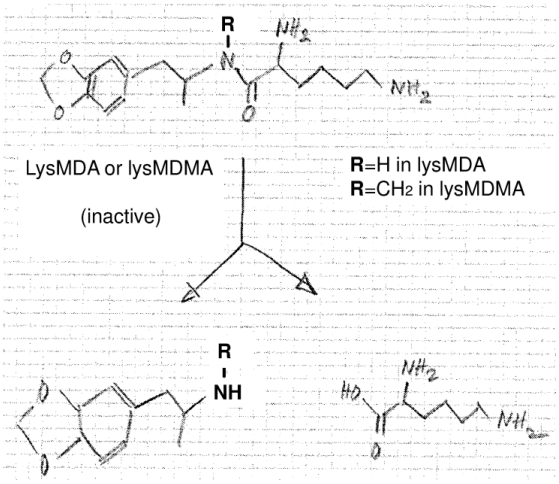


Figure 2:

Fig. 2



2. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009).

From **claim 1**: "A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt thereof, said method comprising orally administering to said subject a prodrug or a salt thereof said **prodrug comprising said amphetamine covalently bonded to a single amino acid** or to a peptide comprising from 2 to 10 amino acids, whereby the blood levels of said amphetamine achieve a therapeutically effect level but said blood levels do not result in a euphoric effect."

From **paragraph [0096]**: "**The amphetamine, A, can be any of the sympathomimetic phenethylamine**

	derivatives which have central nervous system stimulant activity such as amphetamine, or any derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, **methylenedioxyamphetamine**, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-trimethoxyamphetamine, and **3,4-methylenedioxymethamphetamine**…" From **paragraph [0107]**: "Each amino acid can be any one of the L- or D-enantiomers, preferably L-enantiomers, of the naturally occurring amino acids: alanine (Ala or A), arginine (Arg or R), asparagine (Asn or N), **aspartic acid (Asp or D)**, cysteine (Cys or C), glycine (Gly or G), **glutamic acid (Glu or E**), glutamine (Gln or Q), histidine (His or H), isoleucine (Ile or I), leucine (Leu or L), **lysine (Lys or K)**, methionine (Met or M), proline (Pro or P), phenylalanine (Phe or F), serine (Ser or S), **tryptophan (Trp or W)**, threonine (Thr or T), **tyrosine (Tyr or Y)**, and valine (Val or V)…" 3. MAZUR (1970) "Structure-taste relation of aspartic acid amides" J. Med. Chem. Vol 13(6): 1217-1221.

Table 2 (entry 64):

TABLE II

ASPARTIC ACID AMIDES
Asp-X[a]

No.	X	Yield,[b] %	Mp, °C	[α]D, deg	Formula[c]	Taste
50	HNCH(CH3)CH2C6H5; L-	88 AC	197–198 W	−12 M	C13H18N2O3	50
51	HNCH(CH3)CH2C6H5; D-	98 AC	222–225 E W	+14 W	C13H18N2O3	0
52	HNCH(CH3)CH2C6H5[d]	79 M	164–166 A-W	+34 M	C13H18N2O3	-
53	HNCH2CH2C6H5	70 AC	212–214 P-W	−15 W	C12H16N2O3	0
54	HNCH(C2H5)CH2C6H5	91 AC	158–163 M-ET	+8 M	C14H20N2O3·0.25H2O	5
55	HNC(CH3)2CH2C6H5	96 AC	159–161 W	−16 M	C14H20N2O3	20
56		91 M	223–224 M-W	−6 H	C13H16N2O3	10
57	HNCHCHC6H5; L-	95 M	175–178	+5 M	C13H16N2O3·H2O	-
58	HNCH2CH(CH3)C6H5	70 AC	182–188 W	−20 W	C12H18N2O3	-
59	N(CH3)CH(CH3)CH2C6H5; L-	84 M	164–166	+47 W	C14H20N2O3·0.5H2O	-
60	N(CH3)CH(CH3)CH2C6H5; D-	82 M	185–187	+12 W	C14H20N2O3·0.5H2O	-
61	HNCH(CH3)CH2CH2C6H5	95 AC	190–196 M-W	+16 H	C13H18N2O3	5
62	HNCH(CH3)CH2OC6H5	68 M	180–184 M-W	+11 H	C12H16N2O3	10
63	HNCH2CH2OC6H5	85 AC	184–185 W	−13 H	C11H14N2O3	+
64	HNCH(CH3)CH2C6H3(OCH2O)-3,4	95 M	189–192	+6 M	C13H16N2O5	-
65	HNCH(CH2OH)CH2C6H5; L-	95 AC	237–238 W	−26 AC	C13H18N2O3	+
66	HNCH(CH3)CH(OH)C6H5	98 M	188–190 M	+10 M	C13H18N2O3·0.5H2O	+
67	HNCH(CH3)CH2C6H4OH-4	95 M	160–185	+5 W	C13H18N2O3	+
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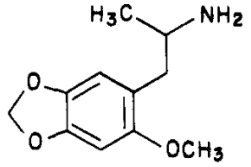
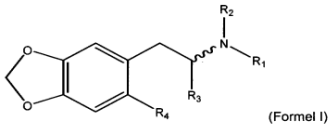
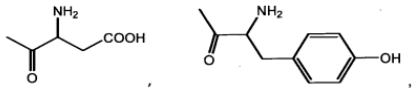
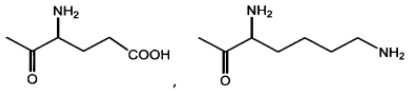
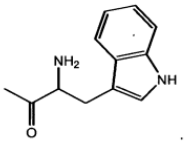
	(0.5 mg/kg, intraperitoneally) from saline…MDAI fully substituted for the discriminative stimulus effects of MDMA (2.5 mg/kg), (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride (5 mg/kg), and cocaine (7.5 mg/kg), but produced only 73% methamphetamine-appropriate responding at a dose that suppressed responding (7.5 mg/kg). MDAI produced tremors at 10 mg/kg in one methamphetamine-trained rat. MDAI produced conditioned place preference from 0.3 to 10 mg/kg. **The effects of MDAI on locomotor activity and drug discrimination were similar to those produced by MDMA, having both psychostimulant-like and hallucinogen-like effects**; thus, MDAI may have similar abuse potential as MDMA. 5. Nichols (1986) "Synthesis and Evaluation of 2,3-Dihydrobenzofuran Analogues of the Hallucinogen 1-(2,5-Dimethoxy-4methylphenyl)-2-aminopropane: Drug Discrimination Studies in Rats" Vol. 29 (2): 302-304. From **page 304, paragraph 2**: "This is all the more difficult to explain in light of the fact that 2-methoxy-4,5-(methylenedioxy)amphetamine (8; MMDA-2) is active  8 and produces clear central effects at an oral dosage of 25 mg of the hydrochloride" 6. Bahji (2019) "Efficacy of 3,4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy for posttraumatic stress disorder: A systematic review and meta-analysis" Progress in Neuropsychopharmacology &Biological Psychiatry, Vol. 96, 109735. From **page 8, conclusions**: "We systematically reviewed and meta-analyzed randomized and quasi-randomized controlled trials measuring the effectiveness and safety MDMA-assisted psychotherapy for treating chronic, treatment-refractory PTSD. We identified five moderate-quality trials demonstrating that MDMA-assisted psychotherapy was associated with significant improvements in PTSD symptoms following intervention that extended long-term with few reported adverse effects. **Taken together, our synthesis suggests that MDMA-assisted psychotherapy is a potentially safe, effective,**

	and durable treatment for individuals with treatment-refractory PTSD."
16. A method for the production of a compound according to claim 1, comprising the steps of: a. preparing a solution of a protected amino acid in solvent I; b. addition of an activating agent dissolved in solvent I under protective gas atmosphere; c. stirring of the mixture under protective gas atmosphere for at least 2 hours at room temperature; e. stirring of the mixture under protective gas atmosphere for at least 2 hours at room temperature; f. stopping the reaction by adding 2% ammonia solution; g1. Concentration of the solvent I; g2. Dissolving the residue in solvent II; h. extraction with 1M HCl, water and saturated saline solution; i. drying of the organic phase over a desiccant at 40-60°C and under vacuum; j. obtaining the crude product; k. purification of the crude product by recrystallization and/or column chromatography; l. obtaining the protected safrylamine peptide; m. deprotection of the protected safrylamine peptide; n. purification of the safrylamine peptide by means of column chromatography; o. obtaining the safrylamine peptide	*From the application of interest's priority document DE 10 2020 123 793.6 (filed 11 September 2020):* From **claim 1**: "1. 3,4-methylenedioxy-amphetamine peptide according to general formula I:  (Formel I) where R1 is selected from the group consisting of:   und  where R2 is selected from the group consisting of: -H or -CH3. where R3 is selected from the group consisting of: -CH3 or -CH2-R4 where R4 is selected from the group consisting of: -H, -OCH3, or R3-CH2- 1. US Priority Doc. No. 63/115,245 of US Pat. Doc. No. 17/518,846 "MDMA PRODRUGS TO ASSIST PSYCHOTHERAPY" (Priority doc filed 18 November 2020). From **claim 1**: "A compound comprising a prodrug including a psychoactive base substance attached to an amino acid." From **claim 3**: "The compound of claim 2, wherein the MDMA or MDMA-like substance is chosen from the group consisting of MDA…MDAI…mixed dopaminergic-serotonergic amphetamine and their N-alkylated analogs..." From **claim 4**: "The compound of claim 1, wherein said amino acid is chosen from the group consisting of lysine, alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine,

leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine."

From **claim 5**: "The compound of claim 1, wherein the amino acid is chosen from the group consisting of natural or synthetic."

Figure 1A:

Fig. 1A

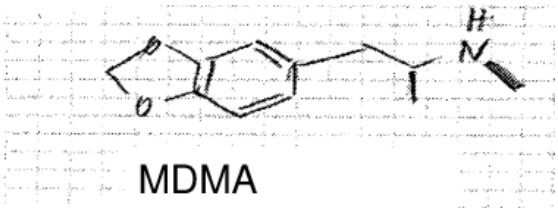
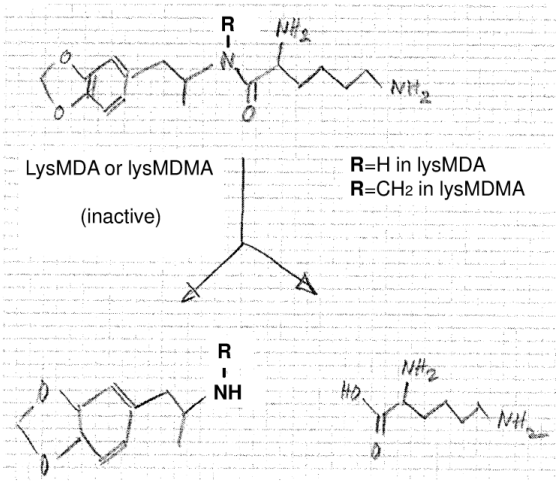


Figure 2:

Fig. 2



2. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009).

From **claim 1**: "A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt thereof, said method comprising orally administering to said subject a prodrug or a salt thereof said **prodrug comprising said amphetamine covalently bonded to a single amino acid** or to a peptide comprising from 2 to 10 amino acids, whereby the blood levels of said amphetamine achieve a therapeutically effect level but said blood levels do not result in a euphoric effect."

From **paragraph [0096]**: "**The amphetamine, A, can be any of the sympathomimetic phenethylamine**

	derivatives which have central nervous system stimulant activity such as amphetamine, or any derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, **methylenedioxyamphetamine**, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-trimethoxyamphetamine, and **3,4-methylenedioxymethamphetamine**…" From **paragraph [0107]**: "Each amino acid can be any one of the L- or D-enantiomers, preferably L-enantiomers, of the naturally occurring amino acids: alanine (Ala or A), arginine (Arg or R), asparagine (Asn or N), **aspartic acid (Asp or D)**, cysteine (Cys or C), glycine (Gly or G), **glutamic acid (Glu or E**), glutamine (Gln or Q), histidine (His or H), isoleucine (Ile or I), leucine (Leu or L), **lysine (Lys or K)**, methionine (Met or M), proline (Pro or P), phenylalanine (Phe or F), serine (Ser or S), **tryptophan (Trp or W)**, threonine (Thr or T), **tyrosine (Tyr or Y)**, and valine (Val or V)…" 3. MAZUR (1970) "Structure-taste relation of aspartic acid amides" J. Med. Chem. Vol 13(6): 1217-1221.

Table 2 (entry 64):

TABLE II

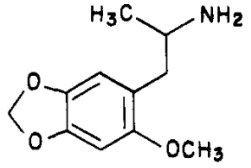
ASPARTIC ACID AMIDES
Asp-X[a]

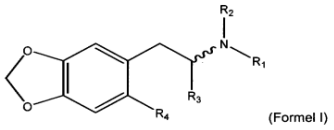
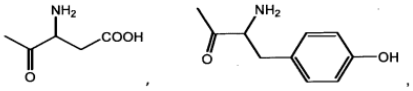
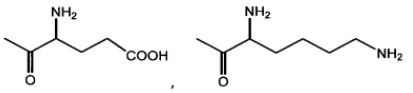
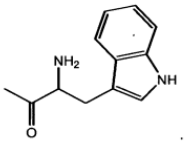
No.	X	Yield,[b] %	Mp, °C	[α]D, deg	Formula[c]	Taste
50	HNCH(CH3)CH2C6H5; L-	88 AC	197–198 W	−12 M	C13H18N2O3	50
51	HNCH(CH3)CH2C6H5; D-	98 AC	222–225 E W	+14 W	C13H18N2O3	0
52	HNCH(CH3)CH2C6H5[d]	79 M	164–166 A-W	+34 M	C13H18N2O3	-
53	HNCH2CH2C6H5	70 AC	212–214 P-W	−15 W	C12H16N2O3	0
54	HNCH(C2H5)CH2C6H5	91 AC	158–163 M-ET	+8 M	C14H20N2O3·0.25H2O	5
55	HNC(CH3)2CH2C6H5	96 AC	159–161 W	−16 M	C14H20N2O3	20
56		91 M	223–224 M-W	−6 H	C13H16N2O3	10
57	HNCHCHC6H5; L-	95 M	175–178	+5 M	C13H16N2O3·H2O	-
58	HNCH2CH(CH3)C6H5	70 AC	182–188 W	−20 W	C12H18N2O3	-
59	N(CH3)CH(CH3)CH2C6H5; L-	84 M	164–166	+47 W	C14H20N2O3·0.5H2O	-
60	N(CH3)CH(CH3)CH2C6H5; D-	82 M	185–187	+12 W	C14H20N2O3·0.5H2O	-
61	HNCH(CH3)CH2CH2C6H5	95 AC	190–196 M-W	+16 H	C13H18N2O3	5
62	HNCH(CH3)CH2OC6H5	68 M	180–184 M-W	+11 H	C12H16N2O3	10
63	HNCH2CH2OC6H5	85 AC	184–185 W	−13 H	C11H14N2O3	+
64	HNCH(CH3)CH2C6H3(OCH2O)-3,4	95 M	189–192	+6 M	C13H16N2O5	-
65	HNCH(CH2OH)CH2C6H5; L-	95 AC	237–238 W	−26 AC	C13H18N2O3	+
66	HNCH(CH3)CH(OH)C6H5	98 M	188–190 M	+10 M	C13H18N2O3·0.5H2O	+
67	HNCH(CH3)CH2C6H4OH-4	95 M	160–185	+5 W	C13H18N2O3	+
68	HNCH2CH2C6H4OH-4	72 AC	209–210 W	−21 W	C12H16N2O3	+
69	HNCH(CH2OH)CH2C6H4OH-4; L-	44 M	212–213 M	−10 H	C13H18N2O3	+
70	HNCH(CH3)CH2C6H4NHSO2CH3-4; L-	96 M	199–208 W	+14 H	C13H19N3O4S	-
71	HNCH(CH3)CH2C6H4F-4	87 M	203–209 M-ET	+9 H	C13H17FN2O3	20
72	HNCH2CH2C6H4F-4	74 M	208–209 W	−6 M	C12H15FN2O3	5
73		85 M	168–180 M-ET	+6 H	C11H16N2O3·0.333H2O	10
74		71 M	195–196 M	−17 M	C10H14N2O3	+
75		96 AC	203–205 M	−22 M	C15H19N3O3	-
76	HNCH(CH3)CH2-c-C6H11; L-	84 AC	184–185 M-W	−19 M	C13H24N2O3	50
77	HNCH(CH3)CH2-c-C6H11; D-	60 M	207–208 M-W	+16 M	C13H24N2O3	5
78	HNCH2CH2-c-C6H11	94 AC	193–202 M-W	+7 AC	C12H22N2O3	10
79	N(CH3)CH(CH3)CH2-c-C6H11; L-	78 M	179–180 P-ET	−14 W	C14H26N2O3·0.25H2O	-
80	N(CH3)CH(CH3)CH2-c-C6H11; D-	64 M	194–196	+1 W	C14H26N2O3	-
81	HN-c-C6H11	91 M	224–227 W	+16 H	C10H18N2O3	-
82	HNCH(CH3)CH2CH2CH3	92 M	190–194 A-W	+9 AC	C7H14N2O3·0.5H2O	0
83	HN(CH2)3CH(CH3)CH3	89 M	222–223 M-W		C10H20N2O3	0
84	HNCH(CH3)CH2CH(CH3)CH3; L-	91 AC	168–168 W	−17 M	C10H20N2O3·0.5H2O	-
85	HNCH(CH3)CH2CH(CH3)CH3; D-	92 AC	201–202 W	+9 M	C10H20N2O3·0.25H2O	-
86	HNCH(C2H5)CH2CH2CH3	93 M	196–200 A-W	+12 AC	C10H20N2O3·H2O	-
87	HN(CH2)3CH3	88 M	200–201 W	+9 AC	C10H20N2O3·0.25H2O	+
88	HNCH(CH3)(CH2)3CH3	98 M	188–193 A-W	+11 AC	C10H20N2O3·0.5H2O	30
89	HN(CH2)4CH3	89 M	200–201 W	+8 AC	C11H22N2O3·0.25H2O	+
90	HNCH(CH3)(CH2)4CH3	95 M	190–194	+7 AC	C11H22N2O3	20
91	HNCH(CH3)CH2CH(CH3)CH2CH3	94 M	162–166 W	−2 M	C11H22N2O3·0.25H2O	+
92	HNCH(CH3)CH2CH2CH(CH3)CH3	94 M	183–188 A-W	+9 AC	C11H22N2O3·0.25H2O	50
93	HNCH(C2H5)(CH2)2CH3	98 M	190–195	+9 AC	C11H22N2O3·0.5H2O	+
94	HNCH(CH3)(CH2)4CH3; L-	94 M	187–189 W	−5 M	C11H22N2O3·H2O	50
95	HNCH(CH3)(CH2)4CH3; L[d]	97 M	213–214 M-W	−5 M	C11H22N2O3·0.5H2O	-
96	HNCH(CH3)(CH2)4CH3; D-	96 M	217–218 M-W	+5 M	C11H22N2O3	0
97	HNCH(CH3)(CH2)4CH3; D[d]	97 M	189–192 W	+6 M	C11H22N2O3	-
98	HNCH(CH3)CH2CH2CH(CH3)CH3; L-	84 M	187–190 W	+23 H	C11H22N2O3·0.5H2O	100
99	HNCH(CH3)CH2CH2CH(CH3)CH3; L[d]	90 M	215–216 M-W	+2 M	C11H22N2O3	0
100	HNCH(CH3)CH2CH2CH(CH3)CH3; D-	96 M	210–213 M-W	−3 M	C11H22N2O3·0.5H2O	+
101	HNCH(CH3)CH2CH2CH(CH3)CH3; D[d]	91 M	192–195 W	−26 H	C11H22N2O3·0.25H2O	-
102	HNCH(CH3)CH2CH2OCH2CH3	77 M	166–170 M-ET	+3 M	C10H20N2O4·0.25H2O	10
103	HNCH(CH3)(CH2)5CH3	85 M	180–190	−8 M	C12H24N2O3·0.5H2O	10

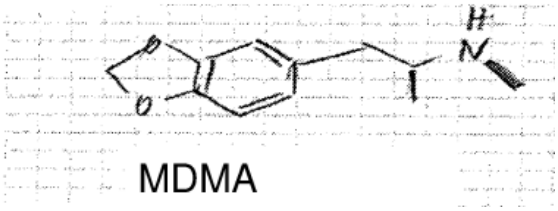
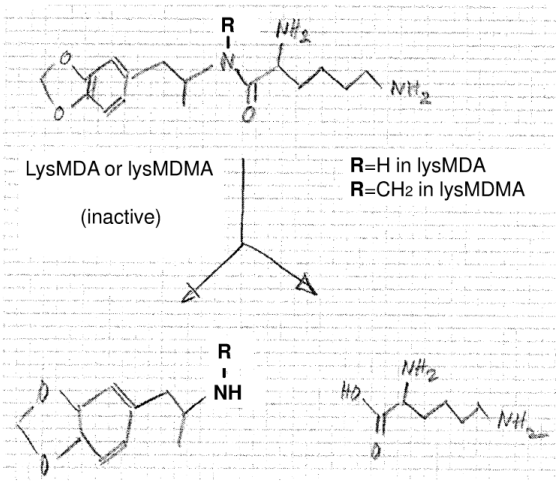
[a] See Table I for abbreviations and explanations. [b] The amide was derived from L-Glu. [c] The amide was derived from DL-Asp. [d] The amide was derived from D-Asp. [e] All compounds were analyzed for C, H, N.

4. Gatch (2016) “Locomotor, discriminative stimulus, and place conditioning effects of MDAI in rodents” Behavioral Pharmacology, Vol 27 (6): 497-505.

From **abstract**: “5,6-Methylenedioxy-2-aminoindane (MDAI) has become a common substitute for (±)-3,4-methylenedioxymethamphetamine (MDMA) in Ecstasy. **MDAI is known to produce MDMA-like discriminative stimulus effects**, but it is not known whether MDAI has psychostimulant or hallucinogen-like effects. MDAI was tested for locomotor stimulant effects in mice and subsequently for discriminative stimulus effects in rats trained to discriminate cocaine (10 mg/kg, intraperitoneally), methamphetamine (1 mg/kg, intraperitoneally), ±MDMA (1.5 mg/kg, intraperitoneally), or (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride

	(0.5 mg/kg, intraperitoneally) from saline…MDAI fully substituted for the discriminative stimulus effects of MDMA (2.5 mg/kg), (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride (5 mg/kg), and cocaine (7.5 mg/kg), but produced only 73% methamphetamine-appropriate responding at a dose that suppressed responding (7.5 mg/kg). MDAI produced tremors at 10 mg/kg in one methamphetamine-trained rat. MDAI produced conditioned place preference from 0.3 to 10 mg/kg. **The effects of MDAI on locomotor activity and drug discrimination were similar to those produced by MDMA, having both psychostimulant-like and hallucinogen-like effects**; thus, MDAI may have similar abuse potential as MDMA. 5. Nichols (1986) "Synthesis and Evaluation of 2,3-Dihydrobenzofuran Analogues of the Hallucinogen 1-(2,5-Dimethoxy-4methylphenyl)-2-aminopropane: Drug Discrimination Studies in Rats" Vol. 29 (2): 302-304. From **page 304, paragraph 2**: "This is all the more difficult to explain in light of the fact that 2-methoxy-4,5-(methylenedioxy)amphetamine (8; MMDA-2) is active  8 and produces clear central effects at an oral dosage of 25 mg of the hydrochloride" 2. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009). From **paragraph [0173]**: "To a solution of a protected amino acid **succinimidyl ester** (2.0 eq) in 1,4-dioxane (30 mL) was added d-amphetamine sulfate (1.0 eq) and NMM (4.0 eq). The resulting mixture was allowed to stir for 20 h at 20° C. Water (10 mL) was added, and the solution was stirred for 10 minutes prior to removing solvents under reduced pressure. The crude product was dissolved in EtOAc (100 mL) and washed with 2% AcOH aq (3×100 mL), saturated NaHCO3 solution (2×50 mL), and brine (1×100 mL). The organic extract was dried over MgSO4, filtered, and evaporated to dryness to afford the protected amino acid amphetamine conjugate. This intermediate was directly deprotected by adding 4 N HCl in 1,4-dioxane (20 mL). The solution was stirred for 20 h at 25° C. The

	solvent was evaporated, and the product dried in vacuum to afford the corresponding amino acid amphetamine hydrochloride conjugate.”
17. The method of production according to claim 16, wherein: (i) the safrylamine is selected from the group consisting of 3,4-methylenedioxy-N-methylamphetamine (MDMA), 3,4-methylenedioxyamphetamine (MDA), 2-methoxy-4,5-methylenedioxyamphetamine (MMDA-2), and 5,6-methylenedioxy-2-aminoindane (MDAI); and/or (ii) the activating agent is selected from the group consisting of 1,1′-carbonyldiimidazole, triethylamine, diisopropylethylamine, pyridine and 4-dimethylaminopyridine, dicyclohexylcarbodiimide (DCC), diisopropylcarbodiimide (DIC), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC), 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (HATU), and (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (PyBOP), or a combination thereof; and/or (iii) the protected amino acid is selected from the group consisting of N-(9-fluorenylmethyloxycarbonyl)-L-tryptophan, N,N′-di-carbobenzoxy-L-lysine, 1-benzyl-N-carbobenzoxy-L-glutamate, N-carbobenzoxy-L-tyrosine, and 4-benzyl N-carbobenzoxy-L-aspartate; and/or (iv) the solvent I is selected from the group consisting of tetrahydrofuran, 2-methyltetrahydrofuran, and dioxane; and/or (v) the solvent II is selected from the group consisting of diethylether, methyl-tert-butylether, chloroform, and dichloromethane, or a combination thereof; and/or	*From the application of interest’s priority document DE 10 2020 123 793.6 (filed 11 September 2020):* From **claim 1**: “1. 3,4-methylenedioxy-amphetamine peptide according to general formula I:  (Formel I) where R1 is selected from the group consisting of:   und  where R2 is selected from the group consisting of: -H or -CH3. where R3 is selected from the group consisting of: -CH3 or -CH2-R4 where R4 is selected from the group consisting of: -H, -OCH3, or R3-CH2- 1. US Priority Doc. No. 63/115,245 of US Pat. Doc. No. 17/518,846 “MDMA PRODRUGS TO ASSIST PSYCHOTHERAPY” (Priority doc filed 18 November 2020). From **claim 1**: “A compound comprising a prodrug including a psychoactive base substance attached to an amino acid.” From **claim 3**: “The compound of claim 2, wherein the MDMA or MDMA-like substance is chosen from the group consisting of MDA…MDAI…mixed dopaminergic-serotonergic amphetamine and their N-alkylated analogs...” From **claim 4**: “The compound of claim 1, wherein said amino acid is chosen from the group consisting of lysine,

(vi) the yield of the safrylamine peptide is at least 45 wt.-% relative to the starting materials.	alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine." From **claim 5**: "The compound of claim 1, wherein the amino acid is chosen from the group consisting of natural or synthetic." **Figure 1A**: Fig. 1A  **Figure 2**: Fig. 2  2. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009). From **claim 1**: "A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt thereof, said method comprising orally administering to said subject a prodrug or a salt thereof said **prodrug comprising said amphetamine covalently bonded to a single amino acid** or to a peptide comprising from 2 to 10 amino acids, whereby the blood levels of said amphetamine achieve a therapeutically effect level but said blood levels do not result in a euphoric effect."

	From **paragraph [0096]**: "**The amphetamine, A, can be any of the sympathomimetic phenethylamine derivatives which have central nervous system stimulant activity** such as amphetamine, or any derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, **methylenedioxyamphetamine**, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-trimethoxyamphetamine, and **3,4-methylenedioxymethamphetamine**…" From **paragraph [0107]**: "Each amino acid can be any one of the L- or D-enantiomers, preferably L-enantiomers, of the naturally occurring amino acids: alanine (Ala or A), arginine (Arg or R), asparagine (Asn or N), **aspartic acid (Asp or D)**, cysteine (Cys or C), glycine (Gly or G), **glutamic acid (Glu or E**), glutamine (Gln or Q), histidine (His or H), isoleucine (Ile or I), leucine (Leu or L), **lysine (Lys or K)**, methionine (Met or M), proline (Pro or P), phenylalanine (Phe or F), serine (Ser or S), **tryptophan (Trp or W)**, threonine (Thr or T), **tyrosine (Tyr or Y)**, and valine (Val or V)…" 3. MAZUR (1970) "Structure-taste relation of aspartic acid amides" J. Med. Chem. Vol 13(6): 1217-1221.

Table 2 (entry 64):

TABLE II

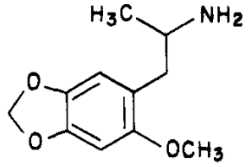
ASPARTIC ACID AMIDES
Asp-X[a]

No.	X	Yield,[b] %	Mp, °C	[α]D, deg	Formula[c]	Taste
50	HNCH(CH3)CH2C6H5; L-	88 AC	197–198 W	−12 M	C13H18N2O3	50
51	HNCH(CH3)CH2C6H5; D-	98 AC	222–225 E W	+14 W	C13H18N2O3	0
52	HNCH(CH3)CH2C6H5[d]	79 M	164–166 A-W	+34 M	C13H18N2O3	-
53	HNCH2CH2C6H5	70 AC	212–214 P-W	−15 W	C12H16N2O3	0
54	HNCH(C2H5)CH2C6H5	91 AC	158–163 M-ET	+8 M	C14H20N2O3·0.25H2O	5
55	HNC(CH3)2CH2C6H5	96 AC	159–161 W	−16 M	C14H20N2O3	20
56		91 M	223–224 M-W	−6 H	C13H16N2O3	10
57	HNCHCHC6H5; L-	95 M	175–178	+5 M	C13H16N2O3·H2O	-
58	HNCH2CH(CH3)C6H5	70 AC	182–188 W	−20 W	C12H18N2O3	-
59	N(CH3)CH(CH3)CH2C6H5; L-	84 M	164–166	+47 W	C14H20N2O3·0.5H2O	-
60	N(CH3)CH(CH3)CH2C6H5; D-	82 M	185–187	+12 W	C14H20N2O3·0.5H2O	-
61	HNCH(CH3)CH2CH2C6H5	95 AC	190–196 M-W	+16 H	C13H18N2O3	5
62	HNCH(CH3)CH2OC6H5	68 M	180–184 M-W	+11 H	C12H16N2O3	10
63	HNCH2CH2OC6H5	85 AC	184–185 W	−13 H	C11H14N2O3	+
64	HNCH(CH3)CH2C6H3(OCH2O)-3,4	95 M	189–192	+6 M	C13H16N2O5	-
65	HNCH(CH2OH)CH2C6H5; L-	95 AC	237–238 W	−26 AC	C13H18N2O3	+
66	HNCH(CH3)CH(OH)C6H5	98 M	188–190 M	+10 M	C13H18N2O3·0.5H2O	+
67	HNCH(CH3)CH2C6H4OH-4	95 M	160–185	+5 W	C13H18N2O3	+
68	HNCH2CH2C6H4OH-4	72 AC	209–210 W	−21 W	C12H16N2O3	+
69	HNCH(CH2OH)CH2C6H4OH-4; L-	44 M	212–213 M	−10 H	C13H18N2O3	+
70	HNCH(CH3)CH2C6H4NHSO2CH3-4; L-	96 M	199–208 W	+14 H	C13H19N3O4S	-
71	HNCH(CH3)CH2C6H4F-4	87 M	203–209 M-ET	+9 H	C13H17FN2O3	20
72	HNCH2CH2C6H4F-4	74 M	208–209 W	−6 M	C12H15FN2O3	5
73		85 M	168–180 M-ET	+6 H	C11H16N2O3·0.333H2O	10
74		71 M	195–196 M	−17 M	C10H14N2O3	+
75		96 AC	203–205 M	−22 M	C15H19N3O3	-
76	HNCH(CH3)CH2-c-C6H11; L-	84 AC	184–185 M-W	−19 M	C13H24N2O3	50
77	HNCH(CH3)CH2-c-C6H11; D-	60 M	207–208 M-W	+16 M	C13H24N2O3	5
78	HNCH2CH2-c-C6H11	94 AC	193–202 M-W	+7 AC	C12H22N2O3	10
79	N(CH3)CH(CH3)CH2-c-C6H11; L-	78 M	179–180 P-ET	−14 W	C14H26N2O3·0.25H2O	-
80	N(CH3)CH(CH3)CH2-c-C6H11; D-	64 M	194–196	+1 W	C14H26N2O3	-
81	HN-c-C6H11	91 M	224–227 W	+16 H	C10H18N2O3	-
82	HNCH(CH3)CH2CH2CH3	92 M	190–194 A-W	+9 AC	C7H14N2O3·0.5H2O	0
83	HN(CH2)3CH(CH3)CH3	89 M	222–223 M-W		C10H20N2O3	0
84	HNCH(CH3)CH2CH(CH3)CH3; L-	91 AC	168–168 W	−17 M	C10H20N2O3·0.5H2O	-
85	HNCH(CH3)CH2CH(CH3)CH3; D-	92 AC	201–202 W	+9 M	C10H20N2O3·0.25H2O	-
86	HNCH(C2H5)CH2CH2CH3	93 M	196–200 A-W	+12 AC	C10H20N2O3·H2O	-
87	HN(CH2)3CH3	88 M	200–201 W	+9 AC	C10H20N2O3·0.25H2O	+
88	HNCH(CH3)(CH2)3CH3	98 M	188–193 A-W	+11 AC	C10H20N2O3·0.5H2O	30
89	HN(CH2)4CH3	89 M	200–201 W	+8 AC	C11H22N2O3·0.25H2O	+
90	HNCH(CH3)(CH2)4CH3	95 M	190–194	+7 AC	C11H22N2O3	20
91	HNCH(CH3)CH2CH(CH3)CH2CH3	94 M	162–166 W	−2 M	C11H22N2O3·0.25H2O	+
92	HNCH(CH3)CH2CH2CH(CH3)CH3	94 M	183–188 A-W	+9 AC	C11H22N2O3·0.25H2O	50
93	HNCH(C2H5)(CH2)2CH3	98 M	190–195	+9 AC	C11H22N2O3·0.5H2O	+
94	HNCH(CH3)(CH2)4CH3; L-	94 M	187–189 W	−5 M	C11H22N2O3·H2O	50
95	HNCH(CH3)(CH2)4CH3; L[d]	97 M	213–214 M-W	−5 M	C11H22N2O3·0.5H2O	-
96	HNCH(CH3)(CH2)4CH3; D-	96 M	217–218 M-W	+5 M	C11H22N2O3	0
97	HNCH(CH3)(CH2)4CH3; D[d]	97 M	189–192 W	+6 M	C11H22N2O3	-
98	HNCH(CH3)CH2CH2CH(CH3)CH3; L-	84 M	187–190 W	+23 H	C11H22N2O3·0.5H2O	100
99	HNCH(CH3)CH2CH2CH(CH3)CH3; L[d]	90 M	215–216 M-W	+2 M	C11H22N2O3	0
100	HNCH(CH3)CH2CH2CH(CH3)CH3; D-	96 M	210–213 M-W	−3 M	C11H22N2O3·0.5H2O	+
101	HNCH(CH3)CH2CH2CH(CH3)CH3; D[d]	91 M	192–195 W	−26 H	C11H22N2O3·0.25H2O	-
102	HNCH(CH3)CH2CH2OCH2CH3	77 M	166–170 M-ET	+3 M	C10H20N2O4·0.25H2O	10
103	HNCH(CH3)(CH2)5CH3	85 M	180–190	−8 M	C12H24N2O3·0.5H2O	10

[a] See Table I for abbreviations and explanations. [b] The amide was derived from L-Glu. [c] The amide was derived from DL-Asp. [d] The amide was derived from D-Asp. [e] All compounds were analyzed for C, H, N.

4. Gatch (2016) “Locomotor, discriminative stimulus, and place conditioning effects of MDAI in rodents” Behavioral Pharmacology, Vol 27 (6): 497-505.

From **abstract**: “5,6-Methylenedioxy-2-aminoindane (MDAI) has become a common substitute for (±)-3,4-methylenedioxymethamphetamine (MDMA) in Ecstasy. **MDAI is known to produce MDMA-like discriminative stimulus effects**, but it is not known whether MDAI has psychostimulant or hallucinogen-like effects. MDAI was tested for locomotor stimulant effects in mice and subsequently for discriminative stimulus effects in rats trained to discriminate cocaine (10 mg/kg, intraperitoneally), methamphetamine (1 mg/kg, intraperitoneally), ±MDMA (1.5 mg/kg, intraperitoneally), or (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride

	(0.5 mg/kg, intraperitoneally) from saline…MDAI fully substituted for the discriminative stimulus effects of MDMA (2.5 mg/kg), (−)-2,5-dimethoxy-4-methylamphetamine hydrochloride (5 mg/kg), and cocaine (7.5 mg/kg), but produced only 73% methamphetamine-appropriate responding at a dose that suppressed responding (7.5 mg/kg). MDAI produced tremors at 10 mg/kg in one methamphetamine-trained rat. MDAI produced conditioned place preference from 0.3 to 10 mg/kg. **The effects of MDAI on locomotor activity and drug discrimination were similar to those produced by MDMA, having both psychostimulant-like and hallucinogen-like effects**; thus, MDAI may have similar abuse potential as MDMA. 5. Nichols (1986) "Synthesis and Evaluation of 2,3-Dihydrobenzofuran Analogues of the Hallucinogen 1-(2,5-Dimethoxy-4methylphenyl)-2-aminopropane: Drug Discrimination Studies in Rats" Vol. 29 (2): 302-304. From **page 304, paragraph 2**: "This is all the more difficult to explain in light of the fact that 2-methoxy-4,5-(methylenedioxy)amphetamine (8; MMDA-2) is active  8 and produces clear central effects at an oral dosage of 25 mg of the hydrochloride"

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APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/024,517	**03/21/2024 11:28:58 AM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Steven Schmid
PATENT CENTER #	64778004	FILING DATE	03/03/2023
CUSTOMER #	–	FIRST NAMED INVENTOR	
INTL. APPLICATION #	-	INTL. FILING DATE	-
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	-

Documents

TOTAL DOCUMENTS: 14

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
Concise-description-generated.pdf		2	Concise Description of Relevance	32 KB
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third-party-preissuance-submission.pdf		3	Third-Party Submission Under 37 CFR 1.290	59 KB
US20230322743.pdf		55	-	844 KB
US20230322743-3P.RELEVANCE.pdf	(1-55)	55	Concise Description of Relevance	827 KB
US20230322743-3P.RELEVANCE.pdf	(1-55)	55	Concise Description of Relevance	827 KB

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63115245 drawings_specification_claims.pdf		45	-	3003 KB
63115245 drawings_specification_claims-NPL.pdf	(1-45)	45	Non Patent Literature	3001 KB
3. MAZUR.pdf		5	-	4367 KB
3. MAZUR-NPL.pdf	(1-5)	5	Non Patent Literature	4363 KB
4. GATCH.pdf		18	-	1084 KB
4. GATCH-NPL.pdf	(1-18)	18	Non Patent Literature	1084 KB
5. NICHOLS.pdf		3	-	2745 KB
5. NICHOLS-NPL.pdf	(1-3)	3	Non Patent Literature	2741 KB
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DOCUMENT	MESSAGE DIGEST(SHA-512)
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Third-party-notification-request.pdf	19BEEED7C51A3CF9D5113451D3C4A95234B42BBCE31F99587F634219344D7D9985DCDBCE2CC854279796B21354CB6A182926F585CF0874735D5B3B488B2C065F
third-party-preissuance-submission.pdf	E2A2B1945CFD8B775111AB8FB9F4FAC822A263E71A756581E33C198367CC63F48FF5A4FE90446638E105E23CEB738357AA96F2C98FD719F9E9B10336EAB620F6

US20230322743.pdf	8537782DD1CF5925F75092F494F59C700E072A40C28F6674B7DE1DB442112E072A32FFB20E5124B893E61EA3496AAD92D4F8580B5FF3BE45A467D24F398B3D7B
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3. MAZUR.pdf	4560795F77F9DDA0B5938FE1A16E99084E70C7FD53690131FD7CF28399F6824AF65B8D99079A6D9AED4221D558DC9D8357A5486951F9B9433E8BBDEFA9DEC5CA
3. MAZUR-NPL.pdf	0B32488C72824972F2FAAAE17ED2CECE5C49F0C5CD4CCF1BD79709E77C6299DAECB4A63EF5E57A9AC1482CF109BFD2C1F0A665FD087DD2BE71CA8DCE688946D7
4. GATCH.pdf	0B89DFBF85699321B9AAA7036D68D777FC77662E08B5497A4377E7ED2581140A401DD9EC3E0B80A0831B98C7553AFB9977D0AB0F928801C2A0255915C99CDC6A
4. GATCH-NPL.pdf	DBA648E1CB2187F3CDDD9B1CC0557B39E696EABCA51A0D75DD14F83B045AB38D95C6642F8B0C32BB229ADC9CD66CBF45BF2BE1B931BFA71D9472F3039AF15012
5. NICHOLS.pdf	67D9B77D080EE5DEF081243F49794EEE89A30D31C751649860EEF5D378A5482B4006F7B1104C9DB9CE6553D56DB3E22AC

	41AE8B6B9DE15C563414F2EAEF5F4F1
5. NICHOLS-NPL.pdf	6E1F1A6DDB6CC3DD0E462D0FF751E6245D4C7E7CB3C684AA25B91897CE78665665CF9E9CB23E7072226DF1E4EBEF50550E170E3D1FA1E96F8F666AD7CD03A43C
6. BAHJI screenshot.pdf	C98EED0288EEC2F08E33E6A3A4CFFB75671D7B42C759ACC653F9560743FCB0D347E5B248F02761FDA83E8DC739D2384477C859C967189F785F814689B2BE4871
6. BAHJI screenshot-NPL.pdf	41861AD506641820640F9A3CADA4433B04237B99B100DDB4901F8ADD4477A64E0AAEC1DE2E349E4709254EBA53964BD28468655738A73EB2BE3E13A314850DE8

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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

National Stage of an International Application under 35 U.S.C. 371

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 #
18/024,517	**03/21/2024 11:28:58 AM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Steven Schmid
PATENT CENTER #	64778004	AUTHORIZED BY	-
CUSTOMER #	–	FILING DATE	03/03/2023
INTL. APPLICATION #	-	INTL. FILING DATE	-
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
CARD / 6258	**E20243KB30429611**	**Steven Schmid**

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.

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

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C.

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