8/24/2021

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Mind Medicine Inc	Confirmation No.: 2828
Serial No.:	18/543,789	Group No.:
Filing or 371(c) Date:	December 18, 2023	Examiner:

Entitled: Synthesis routes to access mdma prodrugs by using controlled and non-controlled intermediates

THIRD-PARTY PRE-ISSUANCE SUBMISSION

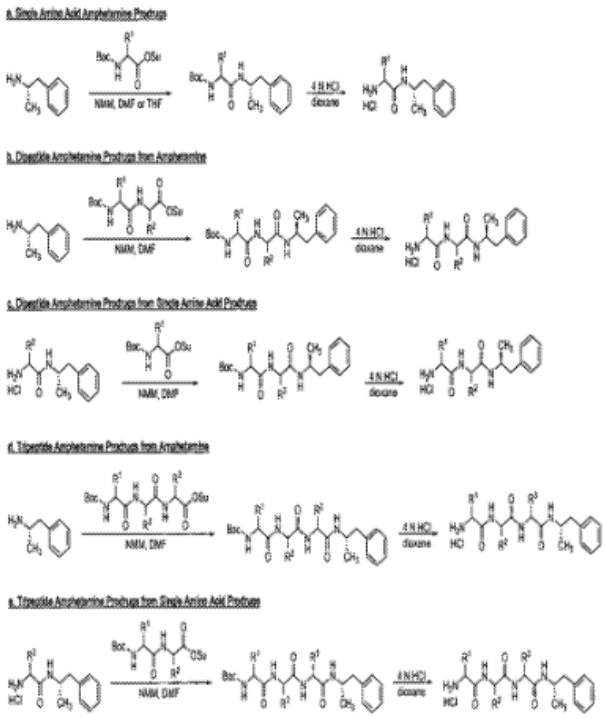
Examiner:

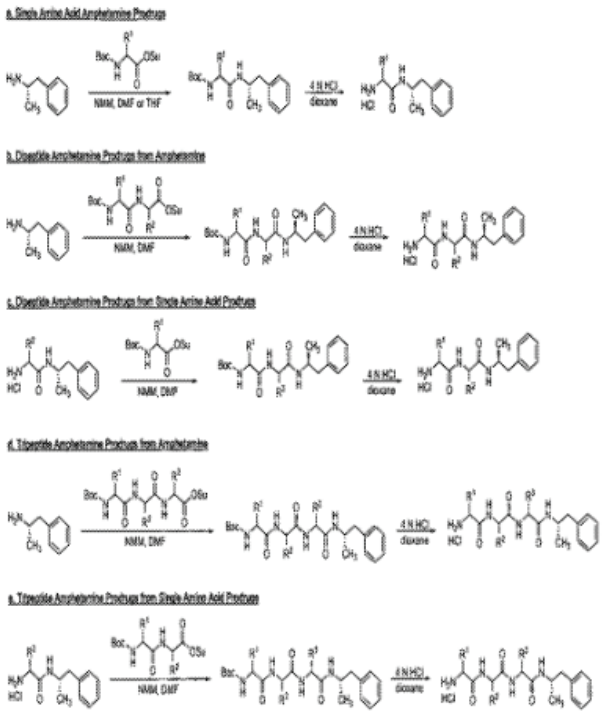
The following documents, which are also identified in the Form PTO/SB/429 filed herewith, are submitted for your consideration as being of potential relevance to the examination of the present application.

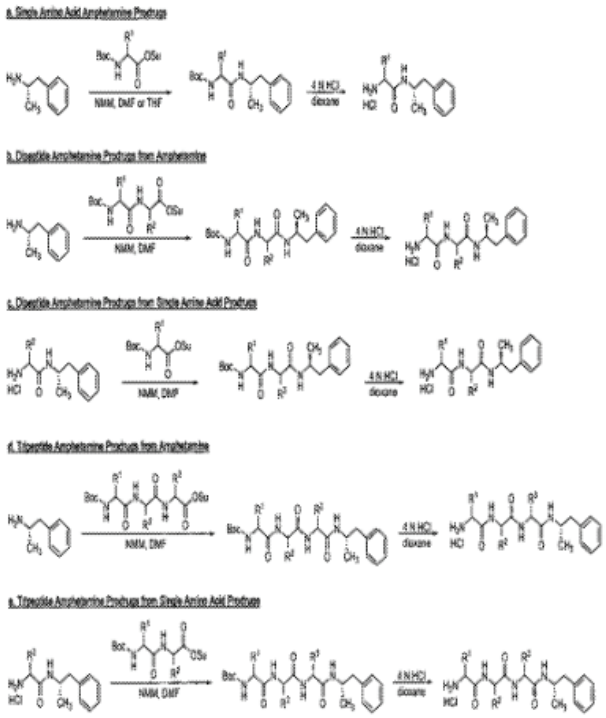
1. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009).
2. DRUGS.COM (2014) "Ecstasy" Drugs.com. Retrieved from July 9th, 2014. URL: https://web.archive.org/web/20140709001207/https://www.drugs.com/illicit/ecstasy.html

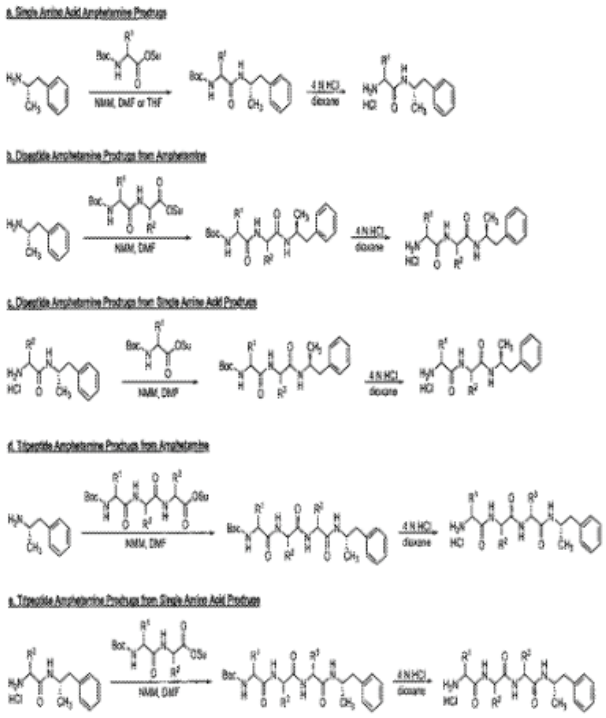
Attached hereto is a claim chart providing a concise description of the relevance of each reference in the document list to the elements of the presently pending claims.

U.S.S.N. 18/543,789 Pending Claims	References
1. A method of synthesizing a pharmacological compound substance including the steps of: attaching a psychoactive base substance to an amino acid; and creating a prodrug with modified pharmacological behavior.	1. 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 [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.**

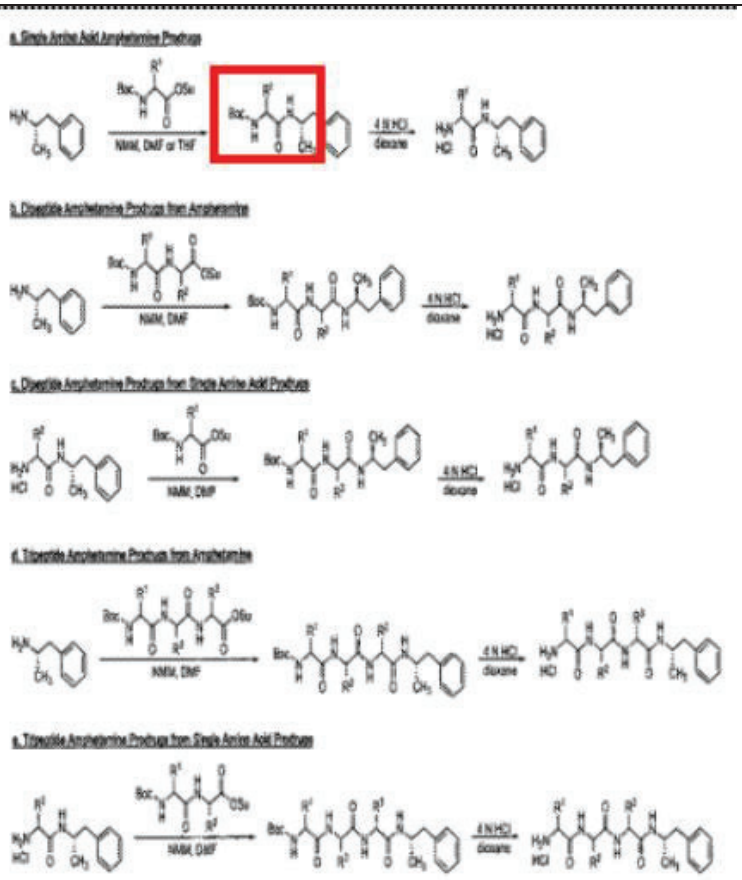
	
2. he method of claim 1, wherein the psychoactive base substance is made of 3,4-methylenedioxymethamphetamine (MDMA) or an MDMA-like substance chosen from the group consisting of 3,4-methylenedioxamphetamine (MDA), 3,4-methylenedioxyethylamphetamine (MDEA), 1-(1,3-benzodioxol-5-yl)methyl-2-butanamine (MBDB), 1-(1,3-benzodioxol-5-yl)-2-aminobutane (BDB), methylone, ethylone, 2F-MDA, 5F-MDA, 6F-MDA, 5,6-methylenedioxy-2-aminoindane (MDAI),	1. 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 [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.**

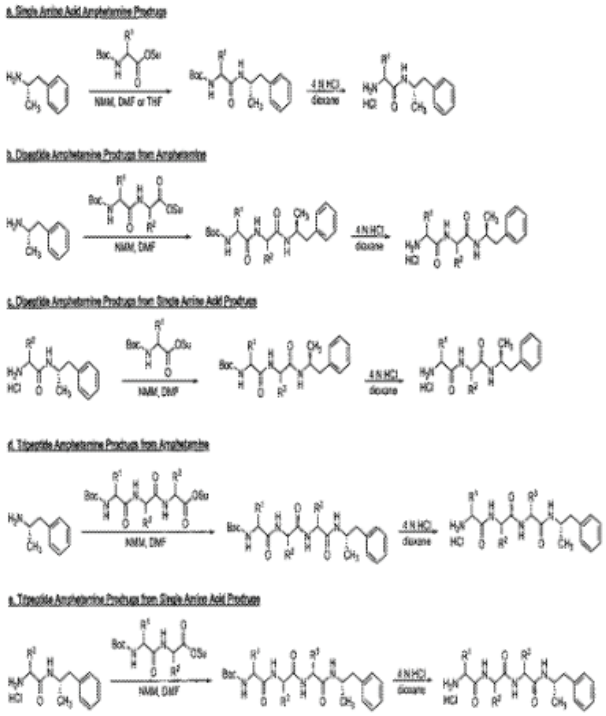
5-iodo-2-aminoindane (5-IAI), 4-(2-aminopropyl)-benzofuran (4-APB), 5-(2-aminopropyl)-benzofuran (5-APB), 6-(2-aminopropyl)-benzofuran (6-APB), 1-(2,3-dihydrobenzofuran-5-yl)-N-methylpropan-2-amine (5-MAPDB), 5-(2-methylaminopropyl)-benzofuran (5-MAPB), mixed dopaminergic-serotonergic amphetamines, N-alkylated analogs of mixed dopaminergic-serotonergic amphetamines, and active metabolites thereof.	
3. The method of claim 1, wherein the 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.	1. 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 [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used**

	to identify favorable conjugates by synthesizing and testing single amino acid conjugates.  From **paragraph [101]: The amphetamine is bound to one or more chemical moieties, denominated X and Z. A chemical moiety can be any moiety that decreases the pharmacological activity of amphetamine while bound to the chemical moiety as compared to unbound (free) amphetamine.** From **paragraph [105]: Preferably, the chemical moiety is a peptide, more particularly a single amino acid, a dipeptide, or a tripeptide. The peptide preferably comprises fewer than 70 amino acids, fewer than 50 amino acids, fewer than 10 amino acids, or fewer than 4 amino acids. When the chemical moiety is one or more amino acids, the amphetamine is preferably bound to lysine, serine, phenylalanine, or glycine. In another embodiment, the amphetamine is preferably bound to lysine, glutamic acid, or leucine. In one embodiment, the amphetamine is bound to lysine and optional additional chemical moieties, e.g., additional amino acids**
4. The method of claim 1, wherein the prodrug made is lysMDA or lysMDMA.	1. 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**

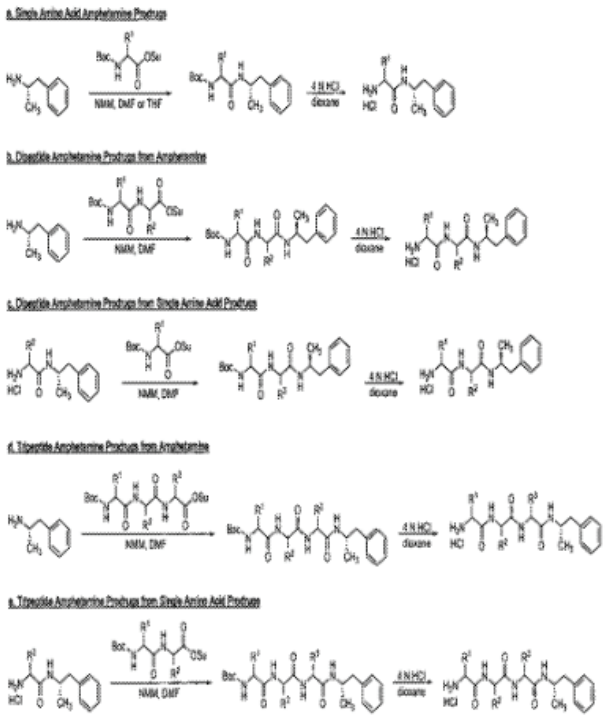
	comprising orally administering to said subject a prodrug or a salt thereof said prodrug comprising said amphetamine covalently bonded to a single amino acid or to a peptide comprising from 2 to 10 amino acids, whereby the blood levels of said amphetamine achieve a therapeutically effect level but said 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 [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.**  From **paragraph [101]: The amphetamine is bound to one or more chemical moieties, denominated X and Z. A chemical moiety can be any moiety that decreases the pharmacological activity of amphetamine while bound to the chemical moiety as compared to unbound (free) amphetamine.**

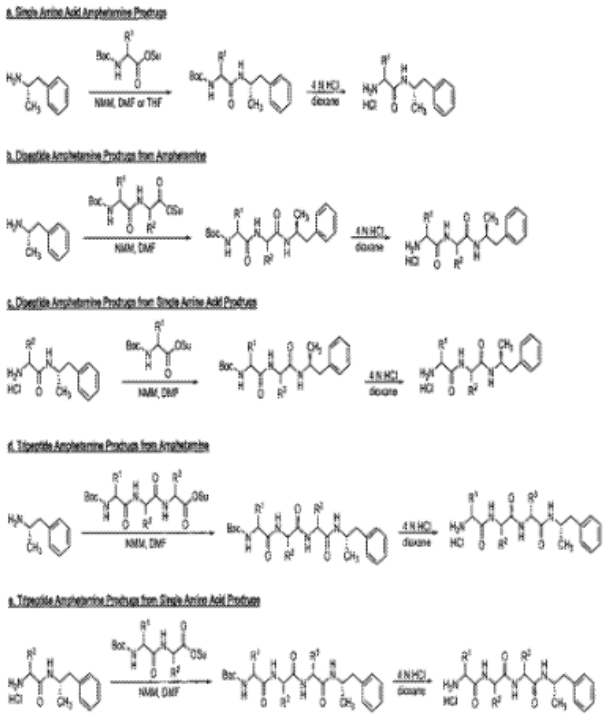
	From **paragraph [105]: Preferably, the chemical moiety is a peptide, more particularly a single amino acid, a dipeptide, or a tripeptide. The peptide preferably comprises fewer than 70 amino acids, fewer than 50 amino acids, fewer than 10 amino acids, or fewer than 4 amino acids. When the chemical moiety is one or more amino acids, the amphetamine is preferably bound to lysine,** serine, phenylalanine, or glycine**. In another embodiment, the amphetamine is preferably bound to lysine,** glutamic acid, or leucine**. In one embodiment, the amphetamine is bound to lysine** and optional additional chemical moieties, e.g., additional amino acids
5. The method of claim 1, wherein the amino acid is attached to an amine group of the psychoactive base substance.	1. 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 [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.**

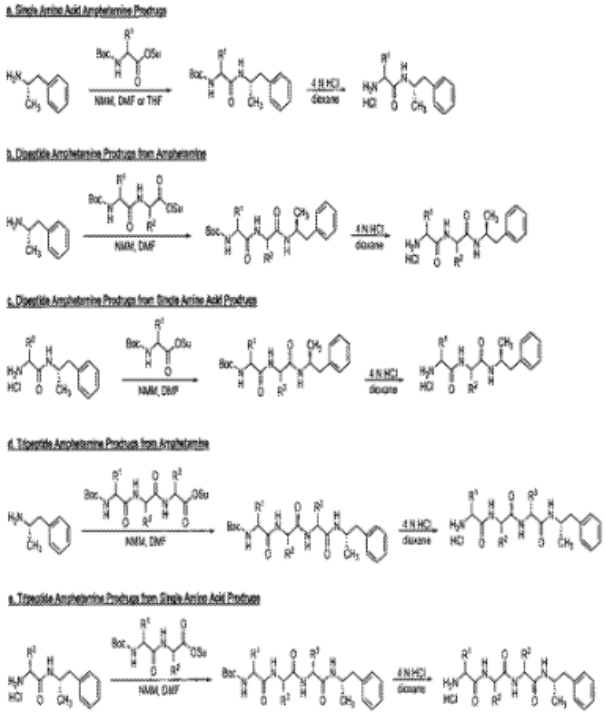
	
6. The method of claim 1, wherein the psychoactive base substance is a controlled substance.	1. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009). From **claim 1**: "**A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically 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 [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.**  2. DRUGS.COM (2014) "Ecstasy" Drugs.com. Retrieved from July 9th, 2014. URL: https://web.archive.org/web/20140709001207/https://www.drugs.com/illicit/ecstasy.html From **What is Ecstasy?: Ecstasy (MDMA, 3,4 methylenedioxymethamphetamine), also commonly called Molly, is a synthetic (lab made), psychoactive drug chemically similar to the stimulant methamphetamine and the hallucinogen mescaline.** It is an illegal drug that acts as both a stimulant and psychedelic, producing an energizing effect, as well as distortions in time and perception and enhanced enjoyment from tactile experiences. **Ecstasy is a Schedule I substance under the Controlled Substances Act, which means that the DEA has determined that it has no medical benefit and a high potential for abuse.**
10. The method of claim 1, wherein the amino acid has an L-configuration.	1. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009).

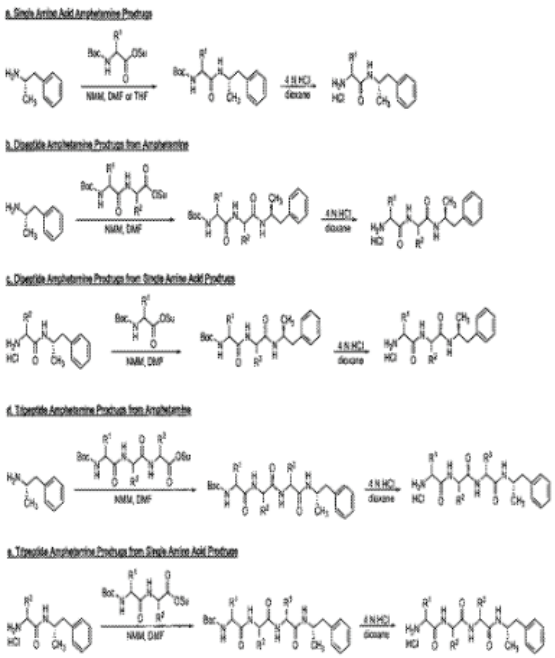
	From **claim 1**: "**A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt thereof, said method comprising orally administering to said subject a prodrug or a salt thereof said prodrug comprising said amphetamine covalently bonded to a single amino 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 [107]: "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)…"** From **paragraph [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.**

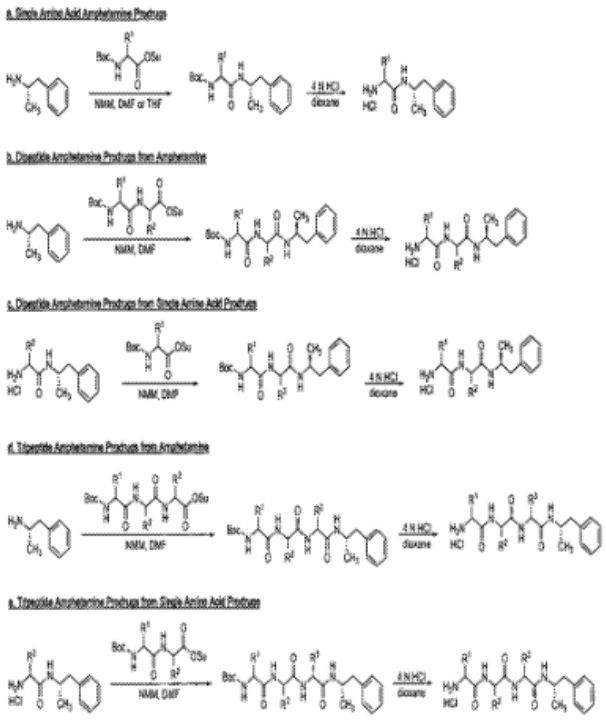
	
11. The method of claim 1, wherein the amino acid has a D-configuration.	1. U.S. Pat. App. Doc. No. 2009/0131335 "ABUSE-RESISTANT AMPHETAMINE PRODRUGS" (Published 21 May 2009). From **claim 1**: "**A method, in a subject, of preventing euphoria due to an amphetamine or a pharmaceutically effective salt 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 [107]: "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),**

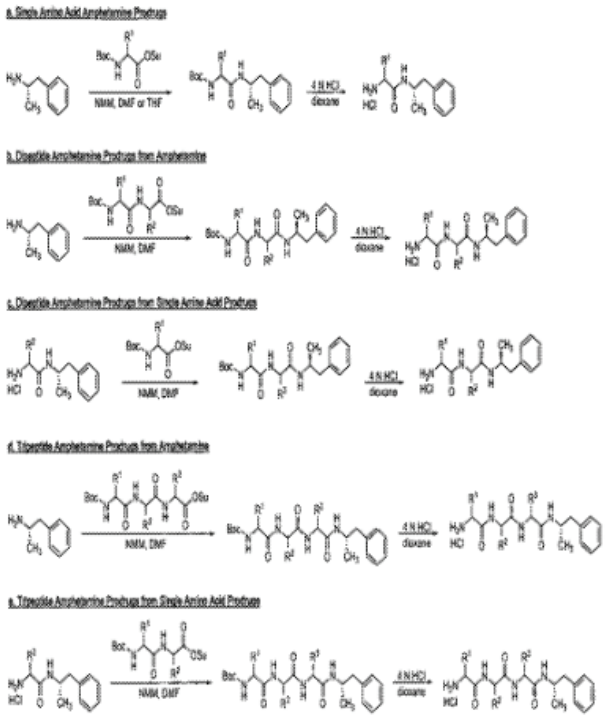
	isoleucine (Ile or I), leucine (Leu or L), lysine (Lys or K), methionine (Met or M), proline (Pro or P), phenylalanine (Phe or F), serine (Ser or S), tryptophan (Trp or W), threonine (Thr or T), tyrosine (Tyr or Y), and valine (Val or V)…" From **paragraph [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.** 
12. A prodrug made by the method of claim 1.	1. 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 [107]: "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)…"** From **paragraph [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.** 
13. The prodrug of claim 12, wherein the psychoactive base substance is made of 3,4-methylenedioxymetham	1. 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**

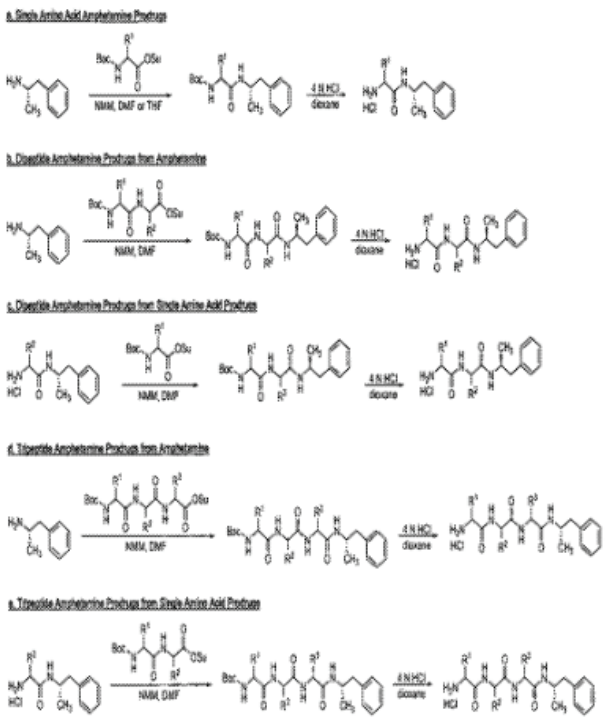
phetamine (MDMA) or an MDMA-like substance chosen from the group consisting of 3,4-methylenedioxamphetamine (MDA), 3,4-methylenedioxyethylamphetamine (MDEA), 1-(1,3-benzodioxol-5-yl)methyl-2-butanamine (MBDB), 1-(1,3-benzodioxol-5-yl)-2-aminobutane (BDB), methylone, ethylone, 2F-MDA, 5F-MDA, 6F-MDA, 5,6-methylenedioxy-2-aminoindane (MDAI), 5-iodo-2-aminoindane (5-IAI), 4-(2-aminopropyl)-benzofuran (4-APB), 5-(2-aminopropyl)-benzofuran (5-APB), 6-(2-aminopropyl)-benzofuran (6-APB), 1-(2,3-dihydrobenzofuran-5-yl)-N-methylpropan-2-amine (5-MAPDB), 5-(2-methylaminopropyl)-benzofuran (5-MAPB), mixed dopaminergic-serotonergic amphetamines, N-alkylated analogs of mixed dopaminergic-serotonergic amphetamines, and active metabolites thereof.	**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 [107]: "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)…"** From **paragraph [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.**

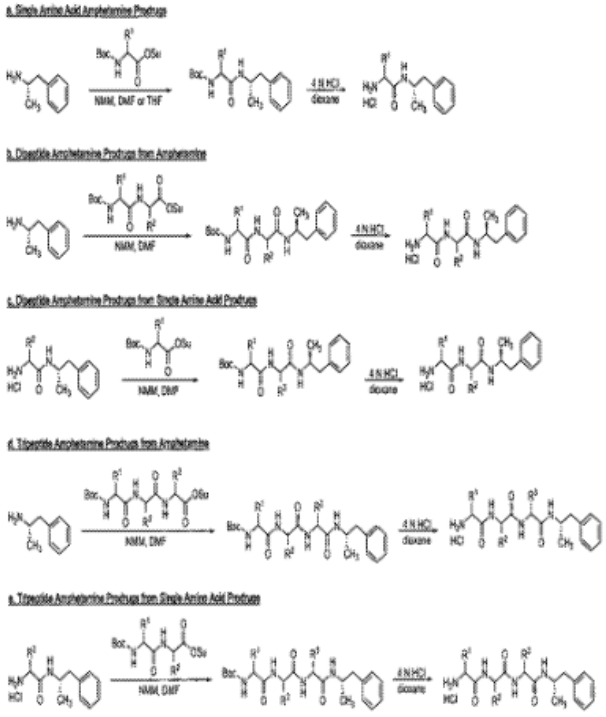
	
14. The prodrug of claim 12, wherein the amino acid is chosen from the group consisting of lysine, alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine.	1. 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 [107]: "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)…" From **paragraph [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.** 
15. A pharmaceutical composition comprising a prodrug of a psychoactive base substance attached to an amino acid and a pharmaceutically acceptable salt.	1. 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 **Field of the Invention: The invention relates to amphetamine compounds, more particularly to amphetamine prodrugs comprising amphetamine covalently bound to a chemical moiety. The invention also relates to pharmaceutical compositions**

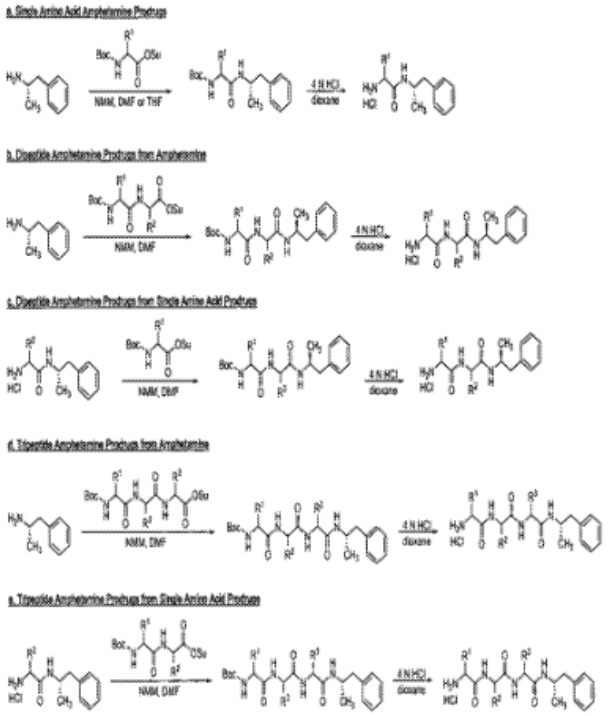
	From **paragraph [0096]**: "**The amphetamine, A, can be any of the sympathomimetic phenethylamine derivatives which have central nervous system stimulant activity** such as amphetamine, or any derivative, analog, or salt thereof. Exemplary amphetamines include, but are not limited to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, **methylenedioxyamphetamine**, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-trimethoxyamphetamine, and **3,4-methylenedioxymethamphetamine**…" From **paragraph [107]: "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)…"** From **paragraph [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.** 

16. The pharmaceutical composition of claim 15, wherein said psychoactive base substance is made of 3,4-methylenedioxymethamphetamine (MDMA) or an MDMA-like substance chosen from the group consisting of 3,4-methylenedioxyamphetamine (MDA), 3,4-methylenedioxyethylamphetamine (MDEA), 1-(1,3-benzodioxol-5-yl)methyl-2-butanamine (MBDB), 1-(1,3-benzodioxol-5-yl)-2-aminobutane (BDB), methylone, ethylone, 2F-MDA, 5F-MDA, 6F-MDA, 5,6-methylenedioxy-2-aminoindane (MDAI), 5-iodo-2-aminoindane (5-IAI), 4-(2-aminopropyl)-benzofuran (4-APB), 5-(2-aminopropyl)-benzofuran (5-APB), 6-(2-aminopropyl)-benzofuran (6-APB), 1-(2,3-dihydrobenzofuran-5-yl)-N-methylpropan-2-amine (5-MAPDB), 5-(2-methylaminopropyl)-benzofuran (5-MAPB), mixed dopaminergic-serotonergic amphetamines, N-alkylated analogs of mixed dopaminergic-serotonergic	1. 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 **Field of the Invention: The invention relates to amphetamine compounds, more particularly to amphetamine prodrugs comprising amphetamine covalently bound to a chemical moiety. The invention also relates to pharmaceutical compositions** 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 [107]: "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)…"** From **paragraph [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.**

amphetamines, and active metabolites thereof.	
17. The pharmaceutical composition of claim 15, 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.	1. 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 **Field of the Invention: The invention relates to amphetamine compounds, more particularly to amphetamine prodrugs comprising amphetamine covalently bound to a chemical moiety. The invention also relates to pharmaceutical compositions** 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 [107]: "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)…"** From **paragraph [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.** 
18. The pharmaceutical composition of claim 15, wherein said pharmaceutically acceptable salt is chosen from the group consisting of sulfate, pyrosulfate, bisulfate, sulfite, bisulfite, phosphate,	1. 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.

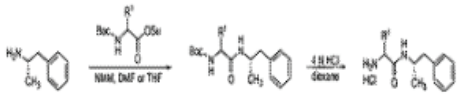
monohydrogen-phosphate, dihydrogenphosphate, metaphosphate, pyro-phosphate, chloride, bromide, iodide, formate, acetate, propionate, decanoate, caprylate, acrylate, isobutyrate, caproate, heptanoate, oxalate, malonate, succinate, suberate, sebacate, fumarate, maleate, benzoate, phthalate, malate, sulfonate, phenylacetate, citrate, lactate, glycollate, tartrate, methanesulfonate, propanesulfonate, and mandelate.	From **Field of the Invention: The invention relates to amphetamine compounds, more particularly to amphetamine prodrugs comprising amphetamine covalently bound to a chemical moiety. The invention also relates to pharmaceutical compositions** 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 [0098]: Preferably, the amphetamine is an amphetamine salt. Pharmaceutically acceptable salt**s, e.g., non-toxic, inorganic and organic acid addition salts, are known in the art. Exemplary salts include, but are not limited to, 2-hydroxyethanesulfonate, 2-naphthalenesulfonate, 3-hydroxy-2-naphthoate, 3-phenylpropionate, **acetate**, adipate, alginate, amsonate, aspartate, benzenesulfonate, **benzoate,** besylate, bicarbonate, **bisulfate**, bitartrate, borate, butyrate, calcium edetate, camphorate, camphorsulfonate, camsylate, carbonate, **citrate**, clavulariate, cyclopentanepropionate, digluconate, dodecylsulfate, edetate, edisylate, estolate, esylate, ethanesulfonate, finnarate, gluceptate, glucoheptanoate, gluconate, glutamate, glycerophosphate, glycollylarsanilate, hemisulfate, **heptanoate**, hexafluorophosphate, hexanoate, hexylresorcinate, hydrabamine, **hydrobromide, hydrochloride, hydroiodide,** hydroxynaphthoate, **iodide,** isothionate, **lactate,** lactobionate, laurate, laurylsulphonate, **malate**, **maleate**, **mandelate**, mesylate, methanesulfonate, methylbromide, methylnitrate, methylsulfate, mucate, naphthylate, napsylate, nicotinate, nitrate, N-methylglucamine ammonium salt, oleate, **oxalate**, palmitate, pamoate, pantothenate, pectinate, persulfate, **phosphate**, phosphateldiphosphate, picrate, pivalate, polygalacturonate, **propionate**, p-toluenesulfonate, saccharate, salicylate, stearate, subacetate, **succinate**, **sulfate**, sulfosaliculate, suramate, tannate, **tartrate**, teoclate, thiocyanate, tosylate, triethiodide, undecanoate, and valerate salts, and the like. From **paragraph [107]: "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)…"**

	From **paragraph [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used to identify favorable conjugates by synthesizing and testing single amino acid conjugates.** 
19. The pharmaceutical composition of claim 18, wherein said pharmaceutically acceptable salt contains at least one deuteron or at least fluorine atom, including stereoisomers thereof.	1. 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 **Field of the Invention: The invention relates to amphetamine compounds, more particularly to amphetamine prodrugs comprising amphetamine covalently bound to a chemical moiety. The invention also relates to pharmaceutical compositions** 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

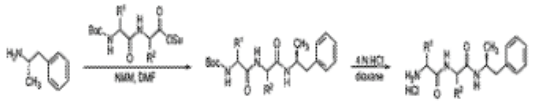
	to, amphetamine, methamphetamine, methylphenidate, p-methoxyamphetamine, **methylenedioxyamphetamine**, 2,5-dimethoxy-4-methylamphetamine, 2,4,5-trimethoxyamphetamine, and **3,4-methylenedioxymethamphetamine**…" From **paragraph [0098]: Preferably, the amphetamine is an amphetamine salt. Pharmaceutically acceptable salts, e.g., non-toxic, inorganic and organic acid addition salts, are known in the art. Exemplary salts include, but are not limited to**, 2-hydroxyethanesulfonate, 2-naphthalenesulfonate, 3-hydroxy-2-naphthoate, 3-phenylpropionate, **acetate**, adipate, alginate, amsonate, aspartate, benzenesulfonate, **benzoate,** besylate, bicarbonate, **bisulfate**, bitartrate, borate, butyrate, calcium edetate, camphorate, camphorsulfonate, camsylate, carbonate, **citrate**, clavulariate, cyclopentanepropionate, digluconate, dodecylsulfate, edetate, edisylate, estolate, esylate, ethanesulfonate, finnarate, gluceptate, glucoheptanoate, gluconate, glutamate, glycerophosphate, glycollylarsanilate, hemisulfate, **heptanoate**, hexafluorophosphate, hexanoate, hexylresorcinate, hydrabamine, **hydrobromide, hydrochloride, hydroiodide,** hydroxynaphthoate, **iodide,** isothionate, **lactate,** lactobionate, laurate, laurylsulphonate, **malate**, **maleate**, **mandelate**, mesylate, methanesulfonate, methylbromide, methylnitrate, methylsulfate, mucate, naphthylate, napsylate, nicotinate, nitrate, N-methylglucamine ammonium salt, oleate, **oxalate**, palmitate, pamoate, pantothenate, pectinate, persulfate, **phosphate**, phosphateldiphosphate, picrate, pivalate, polygalacturonate, **propionate**, p-toluenesulfonate, saccharate, salicylate, stearate, subacetate, **succinate**, **sulfate**, sulfosaliculate, suramate, tannate, **tartrate**, teoclate, thiocyanate, tosylate, triethiodide, undecanoate, and valerate salts, and the like. From **paragraph [107]: "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....** From **paragraph [0172]: Peptide conjugates were synthesized by the general method described in FIG. 1. An iterative approach can be used**

	to identify favorable conjugates by synthesizing and testing single amino acid conjugates.

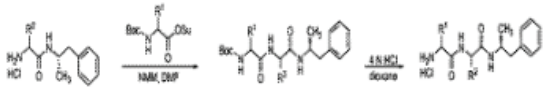
a. Single Amino Acid Amphetamine Prodrugs



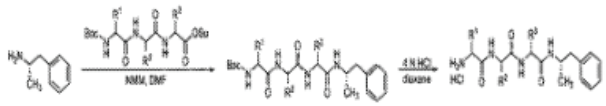
b. Dipeptide Amphetamine Prodrugs from Amphetamine



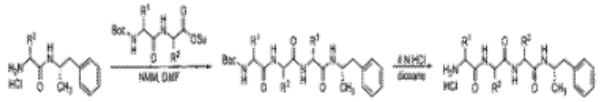
c. Dipeptide Amphetamine Prodrugs from Single Amino Acid Prodrugs



d. Tripeptide Amphetamine Prodrugs from Amphetamine



e. Tripeptide Amphetamine Prodrugs from Single Amino Acid Prodrugs



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APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/543,789	**09/13/2024 01:06:38 PM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Jeremy Rolquin
PATENT CENTER #	67166143	FILING DATE	12/18/2023
CUSTOMER #	–	FIRST NAMED INVENTOR	
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	-

Documents

TOTAL DOCUMENTS: 6

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
Third-party-notification-request.pdf		1	Request for Notification of Non-compliant Third-Party Submission	13 KB
third-party-preissuance-submission.pdf		2	Third-Party Submission Under 37 CFR 1.290	44 KB
Concise-description-generated.pdf		2	Concise Description of Relevance	25 KB
US20240115710 MindMed 3PS Claims Chart.pdf		24	-	348 KB
US20240115710 MindMed 3PS Claims Chart-3P.RELEVANCE.pdf	(1-24)	24	Concise Description of Relevance	346 KB
US20240115710 MindMed 3PS Claims Chart-3P.RELEVANCE.pdf	(1-24)	24	Concise Description of Relevance	346 KB

Ecstasy Embedded.pdf		3	-	92 KB
Ecstasy Embedded-NPL.pdf	(1-3)	3	Non Patent Literature	93 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
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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.