Patents 5,624,910 and 6,121,010. U.S. Patents 5,624,910 and 6,121,010 disclosed ether isoflavone derivatives of daidzein, which were shown to be effective in treating ethanol dependency.

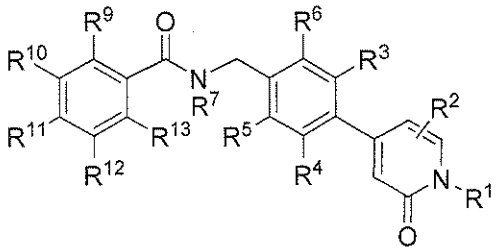
[0011] Mechanistically, daidzein and its derivatives were shown to be potent and selective inhibitors of human mitochondrial aldehyde dehydrogenase (ALDH-2), which is an enzyme involved in the major enzymatic pathway responsible for ethanol metabolism in humans. It appears preferable that daidzein analogues inhibit ALDH-2 selectively relative to the monoamine oxidase (MAO) pathway because daidzein analogues that inhibit both ALDH-2 and MAO exhibited less antidipsotropic activity. Alternatively, WO 2008/014497 disclosed novel isoflavone derivatives that are selective ALDH-2 inhibitors with little effect on the MAO pathway and, thus, are useful for the treatment of alcohol dependency.

[0012] In view of the above-indicated discoveries, a demand has emerged for additional classes of compounds that are safe and effective for the treatment of alcohol dependency, but that are structurally distinct from disulfiram, cyanamide, naltrexone; acamprosate, daidzein, and analogs thereof. Ideally, such additional classes of compounds will also be useful for the treatment of other addictive agents such as cocaine, heroin, and nicotine, and in particular, ameliorate the tendency of abusers to relapse.

SUMMARY

[0013] Surprisingly, it has now been discovered that compounds of Formula (I) as described below, although structurally unrelated to known compounds for the treatment of addictive agents, are nonetheless effective for the treatment of alcohol dependency as determined from the model studies also described herein. Further, the compounds of Formula (I) are effective in the treatment of other addictive agents such as cocaine, heroin, and nicotine. In particular, the compounds of Formula (I) ameliorate the tendency of abusers to relapse. In certain ~~aspects~~embodiments, the compounds of Formula (I) inhibit ALDH-2 selectively relative to the monoamine oxidase (MAO) pathway.

[0014] Accordingly, in certain ~~aspects~~embodiments, is provided compounds of Formula (I):



Formula (I)

wherein:

R^1 is hydrogen, optionally substituted C_{1-6} alkyl, $-CH_2OH$, $-CH_2OP(O)(OR^{20})(OR^{21})$;

R^2 is hydrogen, optionally substituted C_{1-6} alkyl, cycloalkyl, or halo;

each of R^3, R^4, R^5, R^6, R^9, R^{10}, R^{11}, R^{12} and R^{13} is independently hydrogen, hydroxyl, $-OP(O)(OR^{20})(OR^{21})$, $-CH_2OH$, $-CH_2OP(O)(OR^{20})(OR^{21})$, optionally substituted alkyl, optionally substituted alkylene, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, optionally substituted heterocyclyl, aminocarbonyl, acyl, acylamino, -O-(C_1 to C_6-alkyl)-O-(C_1 to C_6-alkyl), cyano, halo, $-SO_2NR^{24}R^{25}$; or $-NR^{24}R^{25}$;

R^7 is hydrogen or optionally substituted C_{1-6} alkyl;

each of R^{20} and R^{21} is independently Na^+, Li^+, K^+, hydrogen, C_{1-6} alkyl; or R^{20} and R^{21} can be combined to represent a single divalent cation Zn^{2+}, Ca^{2+}, or Mg^{2+}.

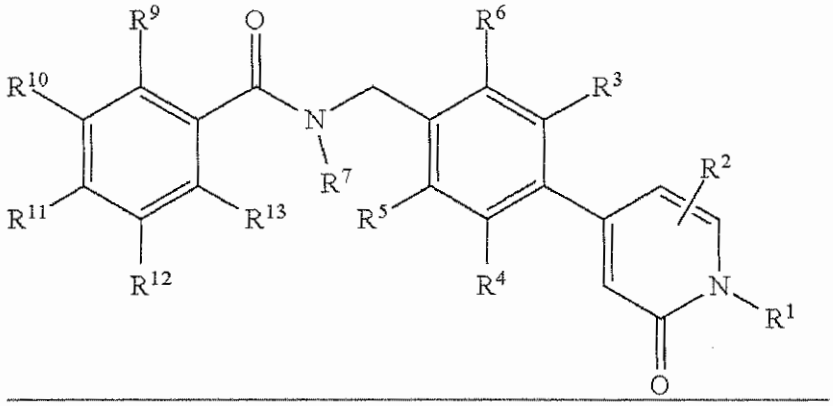
each of R^{22} and R^{23} is independently optionally substituted alkyl, optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, or $-NR^{24}R^{25}$; and

each of R^{24} and R^{25} is independently chosen from hydrogen or C_{1-6} alkyl or when combined together with the nitrogen to which they are attached form a heterocycle; or

a pharmaceutically acceptable salt, ester, single stereoisomer, mixture of stereoisomers, or tautomer thereof.

[0014a] In one aspect, there is provided a compound of formula (I)

Formula (I)



wherein:

R^1 is hydrogen, optionally substituted C_{1-6} alkyl, —CH_2OH, —$CH_2OP(O)(OR^{20})(OR^{21})$;

R^2 is hydrogen, optionally substituted C_{1-6} alkyl, C_3-C_6 cycloalkyl, or halo;

each of R^3, R^4, R^5, R^6, R^9, R^{10}, R^{11}, R^{12} and R^{13} is independently hydrogen, hydroxyl, —$OP(O)(OR^{20})(OR^{21})$, —CH_2OH, —$CH_2OP(O)(OR^{20})(OR^{21})$, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 alkylene, optionally substituted C_2-C_6 alkynyl, optionally substituted C_1-C_6 alkoxy, optionally substituted C_3-C_6 cycloalkyl, aminocarbonyl, acyl, acylamino, —O—(C_1 to C_6-alkyl)—O—(C_1 to C_6-alkyl), cyano, halo, —$SO_2NR^{24}R^{25}$, or —$NR^{24}R^{25}$;

R^7 is hydrogen or optionally substituted C_{1-6} alkyl;

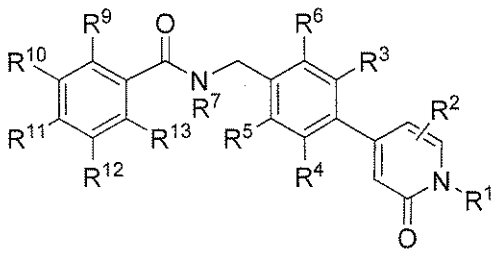
each of R^{20} and R^{21} is independently Na^+, Li^+, K^+, hydrogen, C_{1-6} alkyl; or R^{20} and R^{21} can be combined to represent a single divalent cation Zn^{2+}, Ca^{2+}, or Mg^{2+};

each of R^{22} and R^{23} is independently optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 alkoxy, optionally substituted C_3-C_6 cycloalkyl, optionally substituted aryl, or —$NR^{24}R^{25}$; and

each of R^{24} and R^{25} is independently chosen from hydrogen or C_{1-6} alkyl or when combined together with the nitrogen to which they are attached form a heterocycle; or

a pharmaceutically acceptable salt, ester, single stereoisomer, mixture of stereoisomers, or tautomer thereof.

[0014b] Provided is a compound of Formula (Ia):



Formula (Ia)

wherein:

R^1 is hydrogen, optionally substituted C_{1-6} alkyl, $-CH_2OH$, $-CH_2OP(O)(OR^{20})(OR^{21})$, $-C(O)R^{22}$, or $-SO_2R^{23}$;

R^2 is hydrogen, optionally substituted C_{1-6} alkyl, cycloalkyl, or halo;

each of R^3, R^4, R^5, R^6, R^9, R^{10}, R^{11}, R^{12} and R^{13} is independently hydrogen, hydroxyl, $-OP(O)(OR^{20})(OR^{21})$, $-CH_2OH$, $-CH_2OP(O)(OR^{20})(OR^{21})$, optionally substituted alkyl, optionally substituted alkylene, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, optionally substituted heterocyclyl, aminocarbonyl, acyl, acylamino, -O-(C_1 to C_6-alkyl)-O-(C_1 to C_6-alkyl), cyano, halo, $-SO_2NR^{24}R^{25}$; or $-NR^{24}R^{25}$;

R^7 is hydrogen or optionally substituted C_{1-6} alkyl;

each of R^{20} and R^{21} is independently Na^+, Li^+, K^+, hydrogen, C_{1-6} alkyl; or R^{20} and R^{21} can be combined to represent a single divalent cation Zn^{2+}, Ca^{2+}, or Mg^{2+}.

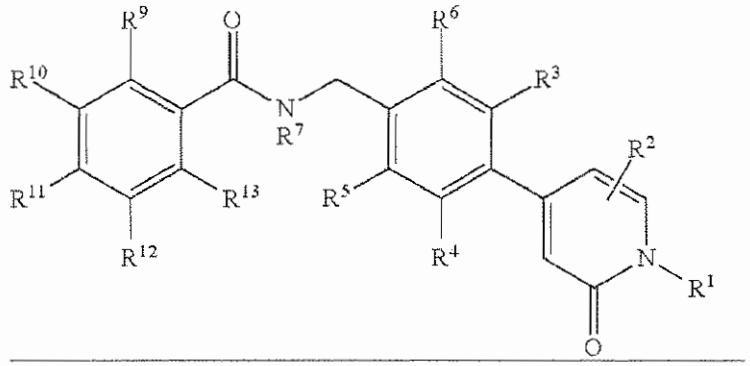
each of R^{22} and R^{23} is independently optionally substituted alkyl, optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, or $-NR^{24}R^{25}$; and

each of R^{24} and R^{25} is independently chosen from hydrogen or C_{1-6} alkyl or when combined together with the nitrogen to which they are attached form a heterocycle; or

a pharmaceutically acceptable salt, ester, single stereoisomer, mixture of stereoisomers, or tautomer thereof.

[0014c] In one aspect, there is provided a compound of Formula (Ia):

Formula (Ia)



wherein:

R^1 is hydrogen, optionally substituted C_{1-6} alkyl, —CH_2OH, —$CH_2OP(O)(OR^{20})(OR^{21})$, —$C(O)R^{22}$, or —$SO_2R^{23}$;

R^2 is hydrogen, optionally substituted C_{1-6} alkyl, C_3-C_6 cycloalkyl, or halo;

each of R^3, R^4, R^5, R^6, R^9, R^{10}, R^{11}, R^{12} and R^{13} is independently hydrogen, hydroxyl, —$OP(O)(OR^{20})(OR^{21})$, —CH_2OH, —$CH_2OP(O)(OR^{20})(OR^{21})$, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 alkylene, optionally substituted C_2-C_6 alkynyl, optionally substituted C_1-C_6 alkoxy, optionally substituted C_3-C_6 cycloalkyl, aminocarbonyl, acyl, acylamino, —O—(C_1 to C_6-alkyl)—O—(C_1 to C_6-alkyl), cyano, halo, —$SO_2NR^{24}R^{25}$; or —$NR^{24}R^{25}$;

R^7 is hydrogen or optionally substituted C_{1-6} alkyl;

each of R^{20} and R^{21} is independently Na^+, Li^+, K^+, hydrogen, C_{1-6} alkyl; or R^{20} and R^{21} can be combined to represent a single divalent cation Zn^{2+}, Ca^{2+}, or Mg^{2+}.

each of R^{22} and R^{23} is independently optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 alkoxy, optionally substituted C_3-C_6 cycloalkyl, optionally substituted aryl, or —$NR^{24}R^{25}$; and

each of R^{24} and R^{25} is independently chosen from hydrogen or C_{1-6} alkyl or when combined together with the nitrogen to which they are attached form a heterocycle; or

a pharmaceutically acceptable salt, ester, single stereoisomer, mixture of stereoisomers, or tautomer thereof.

[0014d] Also provided is a compound of formula (Ib)

R^2 is hydrogen, halo, optionally substituted lower C_{1-6} alkyl, or optionally substituted cycloalkyl;

each of R^3, R^4, R^5, R^6, R^9, R^{10}, R^{11}, R^{12} and R^{13} is independently hydrogen, hydroxyl, $-OP(O)(OR^{20})(OR^{21})$, $-CH_2OH$, $-CH_2OP(O)(OR^{20})(OR^{21})$, aminocarbonyl, acyl, acylamino, -O-(C_1 to C_6-alkyl)-O-(C_1 to C_6-alkyl), cyano, halo, $-SO_2NR^{24}R^{25}$, $-NR^{24}R^{25}$, optionally substituted alkyl, optionally substituted alkylene, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, or optionally substituted heterocyclyl;

R^7 is hydrogen or optionally substituted C_{1-6} alkyl;

each of R^{20} and R^{21} is independently Na^+, Li^+, K^+, hydrogen, C_{1-6} alkyl; or R^{20} and R^{21} can be combined to represent a single divalent cation Zn^{2+}, Ca^{2+}, or Mg^{2+}.

each of R^{22} and R^{23} is independently optionally substituted alkyl, optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, or $-NR^{24}R^{25}$; and

each of R^{24} and R^{25} is independently chosen from hydrogen or C_{1-6} alkyl or when combined together with the nitrogen to which they are attached form a heterocycle; or

a pharmaceutically acceptable salt, ester, single stereoisomer, mixture of stereoisomers, or tautomer thereof.

In certain ~~aspects~~embodiments, the disclosure provides pharmaceutical compositions comprising a therapeutically effective amount of a compound of the disclosure (*e.g.* a compound of Formula (I) or a pharmaceutically acceptable salt, ester, prodrug, stereoisomer, solvate, or hydrate thereof and at least one pharmaceutically acceptable carrier).

[0015a] In one aspect, there is provided a pharmaceutical composition comprising a therapeutically effective amount of the compound as defined herein and a pharmaceutically acceptable carrier.

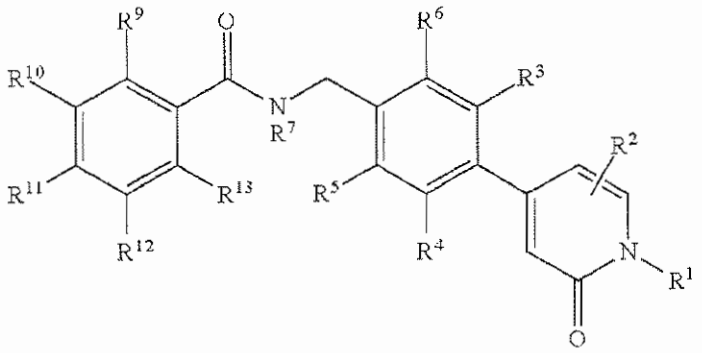
[0016] In certain ~~aspects~~embodiments, is provided methods of using the compounds of Formula (I) in the treatment of addiction to a dopamine-producing agent. The method comprises administering to a mammal in need thereof a therapeutically effective dose of a compound of Formula (I). Such diseases include, but are not limited to, the treatment of dependency upon cocaine, opiates, amphetamines, nicotine, and alcohol.

[0017] Compounds of Formula (I), (Ia), (Ib) or (II) include, but are not limited to:

What is claimed is:

1. A compound of Formula (Ia):

Formula (Ia)



wherein:

R^1 is hydrogen, optionally substituted C_{1-6} alkyl, —CH_2OH, —$CH_2OP(O)(OR^{20})(OR^{21})$, —$C(O)R^{22}$, or —$SO_2R^{23}$;

R^2 is hydrogen, optionally substituted C_{1-6} alkyl, C_3-C_6 cycloalkyl, or halo;

each of R^3, R^4, R^5, R^6, R^9, R^{10}, R^{11}, R^{12} and R^{13} is independently hydrogen, hydroxyl, —OP(O)$(OR^{20})(OR^{21})$, —CH_2OH, —$CH_2OP(O)(OR^{20})(OR^{21})$, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 alkylene, optionally substituted C_2-C_6 alkynyl, optionally substituted C_1-C_6 alkoxy, optionally substituted C_3-C_6 cycloalkyl, aminocarbonyl, acyl, acylamino, —O—(C_1 to C_6-alkyl)—O—(C_1 to C_6-alkyl), cyano, halo, —$SO_2NR^{24}R^{25}$; or —$NR^{24}R^{25}$;

R^7 is hydrogen or optionally substituted C_{1-6} alkyl;

each of R^{20} and R^{21} is independently Na^+, Li^+, K^+, hydrogen, C_{1-6} alkyl; or R^{20} and R^{21} can be combined to represent a single divalent cation Zn^{2+}, Ca^{2+}, or Mg^{2+}.

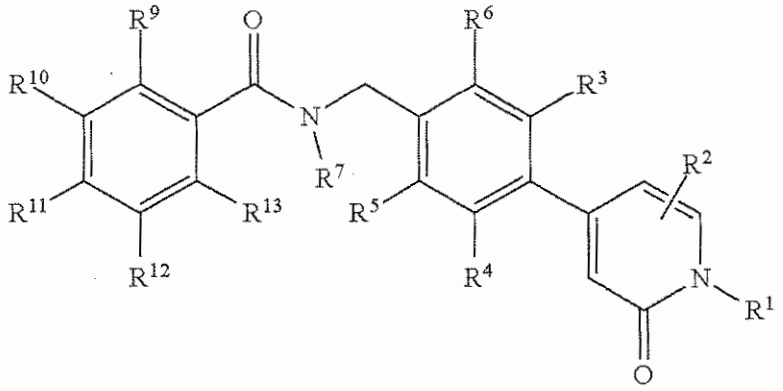
each of R^{22} and R^{23} is independently optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 alkoxy, optionally substituted C_3-C_6 cycloalkyl, optionally substituted aryl, or —$NR^{24}R^{25}$; and

each of R^{24} and R^{25} is independently chosen from hydrogen or C_{1-6} alkyl or when combined together with the nitrogen to which they are attached form a heterocycle; or

a pharmaceutically acceptable salt, ester, single stereoisomer, mixture of stereoisomers, or tautomer thereof.

2. A compound of formula (I)

Formula (I)



wherein:

R^1 is hydrogen, optionally substituted C_{1-6} alkyl, —CH_2OH, —$CH_2OP(O)(OR^{20})(OR^{21})$;

R^2 is hydrogen, optionally substituted C_{1-6} alkyl, C_3-C_6 cycloalkyl, or halo;

each of R^3, R^4, R^5, R^6, R^9, R^{10}, R^{11}, R^{12} and R^{13} is independently hydrogen, hydroxyl, —$OP(O)(OR^{20})(OR^{21})$, —CH_2OH, —$CH_2OP(O)(OR^{20})(OR^{21})$, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 alkylene, optionally substituted C_2-C_6 alkynyl, optionally substituted C_1-C_6 alkoxy, optionally substituted C_3-C_6 cycloalkyl, aminocarbonyl, acyl, acylamino, —O—(C_1 to C_6-alkyl)—O—(C_1 to C_6-alkyl), cyano, halo, —$SO_2NR^{24}R^{25}$; or —$NR^{24}R^{25}$;

R^7 is hydrogen or optionally substituted C_{1-6} alkyl;

each of R^{20} and R^{21} is independently Na^+, Li^+, K^+, hydrogen, C_{1-6} alkyl; or R^{20} and R^{21} can be combined to represent a single divalent cation Zn^{2+}, Ca^{2+}, or Mg^{2+}.

each of R^{22} and R^{23} is independently optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 alkoxy, optionally substituted C_3-C_6 cycloalkyl, optionally substituted aryl, or —$NR^{24}R^{25}$; and

each of R^{24} and R^{25} is independently chosen from hydrogen or C_{1-6} alkyl or when combined together with the nitrogen to which they are attached form a heterocycle; or

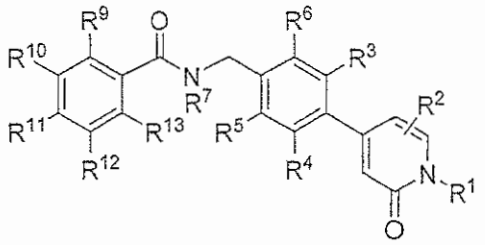
a pharmaceutically acceptable salt, ester, single stereoisomer, mixture of stereoisomers, or tautomer thereof.

3. A pharmaceutical composition comprising a therapeutically effective amount of the compound of any one of claims 1 and a pharmaceutically acceptable carrier.

CLAIMS

What is claimed is:

1. A compound of Formula (Ia):



Formula (Ia)

wherein:

R^1 is hydrogen, optionally substituted C_{1-6} alkyl, $-CH_2OH$, $-CH_2OP(O)(OR^{20})(OR^{21})$, $-C(O)R^{22}$, or $-SO_2R^{23}$;

R^2 is hydrogen, optionally substituted C_{1-6} alkyl, cycloalkyl, or halo;

each of R^3, R^4, R^5, R^6, R^9, R^{10}, R^{11}, R^{12} and R^{13} is independently hydrogen, hydroxyl, $-OP(O)(OR^{20})(OR^{21})$, $-CH_2OH$, $-CH_2OP(O)(OR^{20})(OR^{21})$, optionally substituted alkyl, optionally substituted alkylene, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, optionally substituted heterocyclyl, aminocarbonyl, acyl, acylamino, -O-(C_1 to C_6-alkyl)-O-(C_1 to C_6-alkyl), cyano, halo, $-SO_2NR^{24}R^{25}$; or $-NR^{24}R^{25}$;

R^7 is hydrogen or optionally substituted C_{1-6} alkyl;

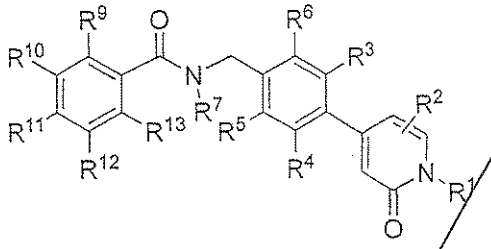
each of R^{20} and R^{21} is independently Na^+, Li^+, K^+, hydrogen, C_{1-6} alkyl; or R^{20} and R^{21} can be combined to represent a single divalent cation Zn^{2+}, Ca^{2+}, or Mg^{2+}.

each of R^{22} and R^{23} is independently optionally substituted alkyl, optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, or $-NR^{24}R^{25}$; and

each of R^{24} and R^{25} is independently chosen from hydrogen or C_{1-6} alkyl or when combined together with the nitrogen to which they are attached form a heterocycle; or

a pharmaceutically acceptable salt, ester, single stereoisomer, mixture of stereoisomers, or tautomer thereof.

2. A compound of formula (I)



Formula (I)

wherein:

R^1 is hydrogen, optionally substituted C_{1-6} alkyl, $-CH_2OH$, $-CH_2OP(O)(OR^{20})(OR^{21})$;

R^2 is hydrogen, optionally substituted C_{1-6} alkyl, cycloalkyl, or halo;

each of R^3, R^4, R^5, R^6, R^9, R^{10}, R^{11}, R^{12} and R^{13} is independently hydrogen, hydroxyl, $-OP(O)(OR^{20})(OR^{21})$, $-CH_2OH$, $-CH_2OP(O)(OR^{20})(OR^{21})$, optionally substituted alkyl, optionally substituted alkylene, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, optionally substituted heterocyclyl, aminocarbonyl, acyl, acylamino, -O-(C_1 to C_6-alkyl)-O-(C_1 to C_6-alkyl), cyano, halo, $-SO_2NR^{24}R^{25}$; or $-NR^{24}R^{25}$;

R^7 is hydrogen or optionally substituted C_{1-6} alkyl;

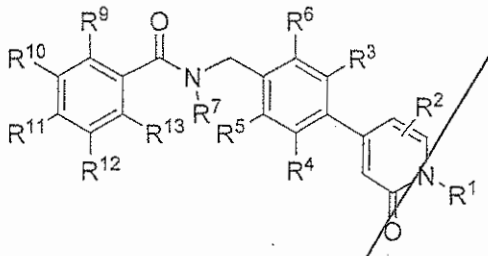
each of R^{20} and R^{21} is independently Na^+, Li^+, K^+, hydrogen, C_{1-6} alkyl; or R^{20} and R^{21} can be combined to represent a single divalent cation Zn^{2+}, Ca^{2+}, or Mg^{2+}.

each of R^{22} and R^{23} is independently optionally substituted alkyl, optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, or $-NR^{24}R^{25}$; and

each of R^{24} and R^{25} is independently chosen from hydrogen or C_{1-6} alkyl or when combined together with the nitrogen to which they are attached form a heterocycle; or

a pharmaceutically acceptable salt, ester, single stereoisomer, mixture of stereoisomers, or tautomer thereof.

3. A compound of formula (Ib)



Formula (Ib)

wherein:

R^1 is hydrogen, C_{1-6} alkyl, $-CH_2OR^{22}$, $-CH_2OP(O)(OR^{20})(OR^{21})$;

R^2 is hydrogen, cyano, C_{1-6} alkyl, C_3-C_6 cycloalkyl, or halo;

each of R^3, R^4, R^5, R^6, R^9, R^{10}, R^{11}, R^{12} and R^{13} is independently hydrogen, halo, C_1-C_6 alky, hydroxyl, or $-CH_2OR^{22}$;

R^7 is hydrogen or C_{1-6} alkyl;

each of R^{20} and R^{21} is independently Na^+, Li^+, K^+, hydrogen, or C_{1-6} alkyl;

each R^{22} is independently hydrogen, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, phenyl or benzyl; or

a pharmaceutically acceptable salt, single stereoisomer, mixture of stereoisomers, or tautomer thereof.

4. The compound of claim 2, wherein R^1 is hydrogen.

5. The compound of claim 2, wherein R^1 is C_{1-6} alkyl.

6. The compound of claim 2, wherein R^1 is methyl.

7. The compound of claim 2, wherein R^1 is $-CH_2OP(O)(OR^{20})(OR^{21})$; and each of R^{20} and R^{21} is independently Na^+, Li^+, K^+, or hydrogen.

8. The compound of any one of claims 2, wherein R^2 is hydrogen, C_{1-6} alkyl, or halo.

9. The compound of any one of claims 2, wherein R^2 is methyl, fluoro or chloro.

10. The compound of any one of claims 2, wherein each of R^3, R^4, R^5, and R^6 is independently hydrogen, C_{1-6} alkyl, or halo.

11. The compound of any one of claims 2, wherein one of R^3, R^4, R^5, or R^6 is methyl or fluoro.

12. The compound of any one of claims 2, wherein R^7 is hydrogen or methyl.

13. The compound of any one of claims 2, wherein at least one of R^9 and R^{13} is not hydrogen.

14. The compound of any one of claims 2, wherein at least one of R^9 and R^{13} is halo or C_{1-6} alkyl.

15. The compound of any one of claims 2, wherein each of R^9 and R^{13} is independently chloro or methyl.

16. The compound of any one of claims 2, wherein each of R^{10} and R^{12} is independently hydrogen, chloro, fluoro, or methyl.

17. The compound of any one of claims 2, wherein R^{10}, R^{11} and R^{12} are each hydrogen.

18. The compound of any one of claims 2, wherein R^{11} is -O-(C_1 to C_6-alkyl)-O-(C_1 to C_6-alkyl).

19. The compound of any one of claims 2, wherein R^{11} is $-OCH_2CH_2OCH_3$.

20. The compound of claim 2, wherein:

R^1 is hydrogen, methyl, or $-CH_2OP(O)(OR^{20})(OR^{21})$;

R^2 is hydrogen, methyl, or fluoro;

each of R^3 or R^4 is independently hydrogen or methyl;

each of R^5 and R^6 is independently hydrogen or fluoro;

R^7 is hydrogen;

R^9 is hydrogen, chloro, fluoro, or methyl;

R^{10} is hydrogen or fluoro;

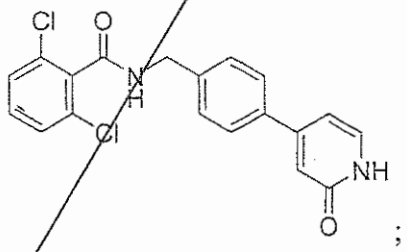
R^{11} is hydrogen or $-OCH_2CH_2OCH_3$;

R^{12} is hydrogen or fluoro;

R^{13} is hydrogen, chloro, fluoro, or methyl; and

each of R^{20} and R^{21} is independently Na^+, Li^+, K^+, or hydrogen.

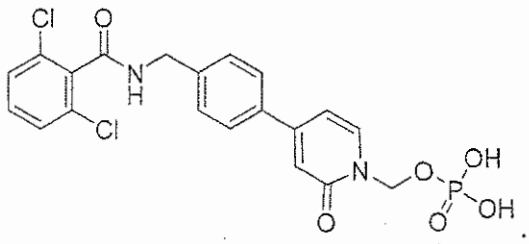
21. The compound of claim 2, wherein the structure is:



;

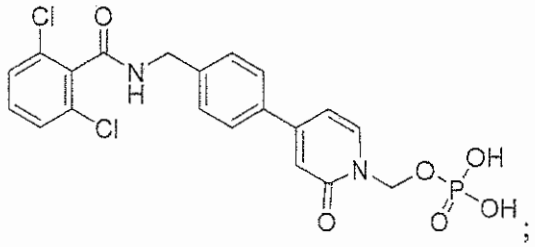
or a pharmaceutically acceptable salt, or tautomer thereof.

22. The compound of claim 2, wherein the structure is:



.

23. The compound of claim 2, wherein the structure is:



or a pharmaceutically acceptable salt, ester, or tautomer thereof.

24. A compound selected from the group consisting of:

2,6-dichloro-4-(2-methoxyethoxy)-*N*-(4-(2-oxo-1,2-dihydropyridin-4-yl) benzyl)benzamide;

2,6-dichloro-*N*-[4-(2-oxo-1,2-dihydro-pyridin-4-yl)-benzyl]-benzamide;

2-chloro-3-fluoro-*N*-(4-(2-oxo-1,2-dihydropyridin-4-yl)benzyl)benzamide;

2-chloro-6-methyl-*N*-(4-(2-oxo-1,2-dihydropyridin-4-yl)benzyl)benzamide;

2,6-dimethyl-*N*-(4-(2-oxo-1,2-dihydropyridin-4-yl)benzyl)benzamide;

2,6-dichloro-*N*-[4-(6-methyl-2-oxo-1,2-dihydro-pyridin-4-yl)-benzyl]-benzamide;

2-chloro-3,6-difluoro-*N*-(4-(2-oxo-1,2-dihydropyridin-4-yl)benzyl)benzamide;

2,6-dichloro-*N*-(3-methyl-4-(2-oxo-1,2-dihydropyridin-4-yl)benzyl)benzamide);

2,6-dichloro-*N*-(4-(1-methyl-2-oxo-1,2-dihydropyridin-4-yl)benzyl)benzamide;

2,6-difluoro-*N*-(4-(2-oxo-1,2-dihydropyridin-4-yl)benzyl)benzamide;

2-chloro-6-fluoro-*N*-(4-(2-oxo-1,2-dihydropyridin-4-yl)benzyl)benzamide;

2,6-dichloro-*N*-(2-fluoro-4-(2-oxo-1,2-dihydropyridin-4-yl)benzyl)benzamide;

2,6-dichloro-*N*-(4-(5-fluoro-2-oxo-1,2-dihydropyridin-4-yl)benzyl)benzamide; and

phosphoric acid mono-(4-{4-[(2,6-dichloro-benzoylamino)-methyl]-phenyl}-2-oxo-2H -pyridin-1-ylmethyl) ester;

2,6-dimethyl-N-(4-(2-oxopiperidin-4-yl)benzyl)benzamide; or

a pharmaceutically acceptable salt, single stereoisomer, mixture of stereoisomers, or tautomer thereof.

25. A pharmaceutical composition comprising a therapeutically effective amount of the compound of any one of claims 2-24 and a pharmaceutically acceptable carrier.

26. A method of treating chemical dependency on a dopamine-producing agent, comprising administering a therapeutically effective dose of the compound of any one of claims 2-24 to a mammal in need thereof.

27. The method of claim 26, wherein the dopamine-producing agent is selected from the group consisting of cocaine, opiates, amphetamines, nicotine, and alcohol.

28. A method of decreasing alcohol consumption in a mammal comprising administering a therapeutically effective amount of a compound according to any one of claims 2-24 or a pharmaceutical acceptable salt, or prodrug thereof to a mammal in need thereof.

29. A method of treating obesity in a mammal comprising administering a therapeutically effective amount of a compound according to any one of claims 2-24 or a pharmaceutically acceptable salt or prodrug thereof to a mammal in need thereof.

30. A compound according to any one of claims 2-24 for use in therapy.

31. Use of a compound according to any one of claims 2-24 for the manufacture of a medicament for the treatment of diseases related to addiction to dopamine producing agents.