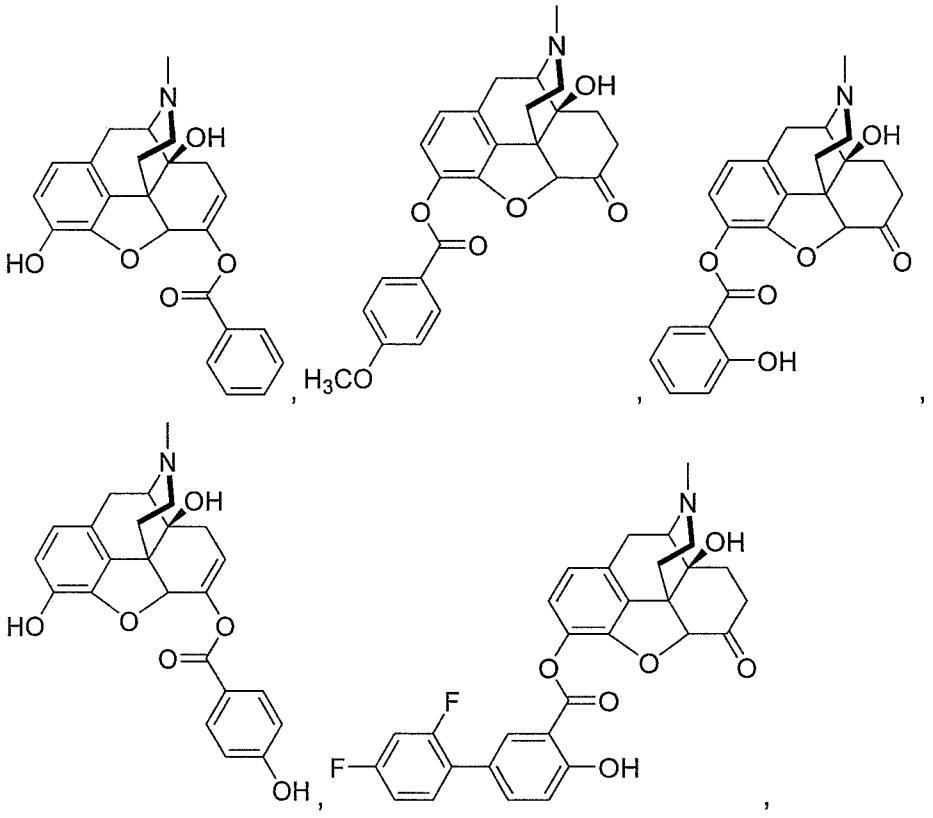
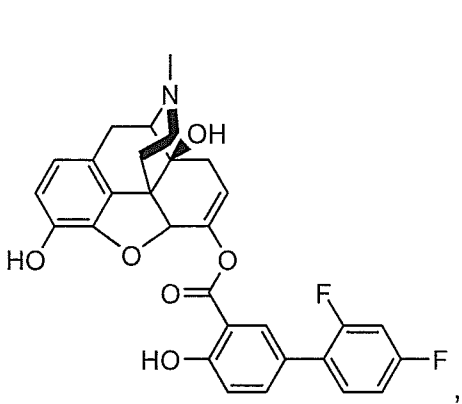
condition (such as addiction) which can be treated by inhibiting binding of at least one opioid to the opioid receptors of the patient, comprising the step of orally administering to the patient a therapeutically or pharmaceutically effective amount of at least one conjugate of oxymorphone disclosed and/or claimed herein.

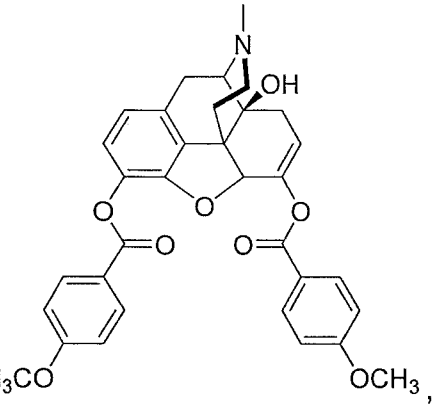
[0032a] In a further aspect, the present technology provides the use of a therapeutically effective amount of at least one composition as described herein, in the manufacture of a medicament for treating a patient having a disease, disorder or condition mediated by binding of at least one opioid to one or more opioid receptors of the patient.

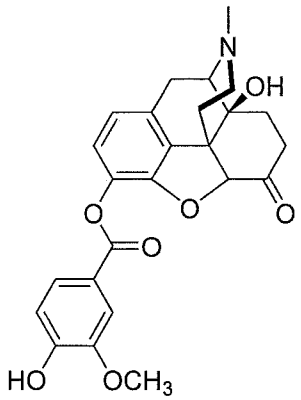
[0033] In a yet further aspect, the present technology provides at least one pharmaceutical kit including a specified amount of individual doses in a package containing a therapeutically or pharmaceutically effective amount of at least one conjugate of oxymorphone described and/or claimed herein. In some aspects, the kits of the presently described technology can further include one or more instructions regarding use of the kit in a method or manner for treating or preventing drug withdrawal symptoms or pain in a human or animal patient.

[0033a] In a yet further aspect, the present technology provides a compound selected from the group consisting of





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and salts thereof.

[0033b] In a yet further aspect, the present technology provides a composition comprising at least one compound as described herein, a salt thereof, or a combination thereof.

BRIEF DESCRIPTION OF SEVERAL VIEWS OF THE DRAWINGS

[0034] Figure 1 provides chemical structures of hydroxybenzoic acids and benzoic acid derivatives for use in the making of the conjugates of the present technology.

[0035] Figure 2 provides chemical structures of aminobenzoic acids for use in the making of the conjugates of the present technology.

[0036] Figure 3 provides chemical structures of aminohydroxybenzoic acids for use in the making of conjugates of the present technology.

[0037] Figure 4 provides chemical structures of heteroaryl carboxylic acids for use in the making of conjugates of the present technology.

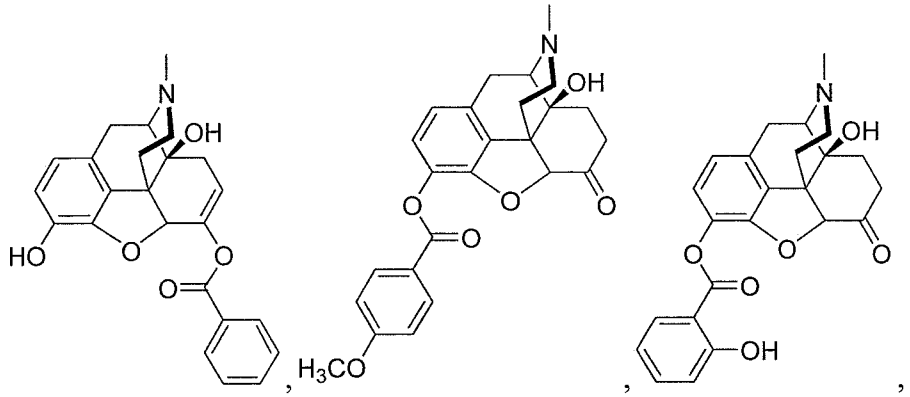
[0038] Figure 5 provides chemical structures of phenylacetates for use in the making of conjugates of the present technology.

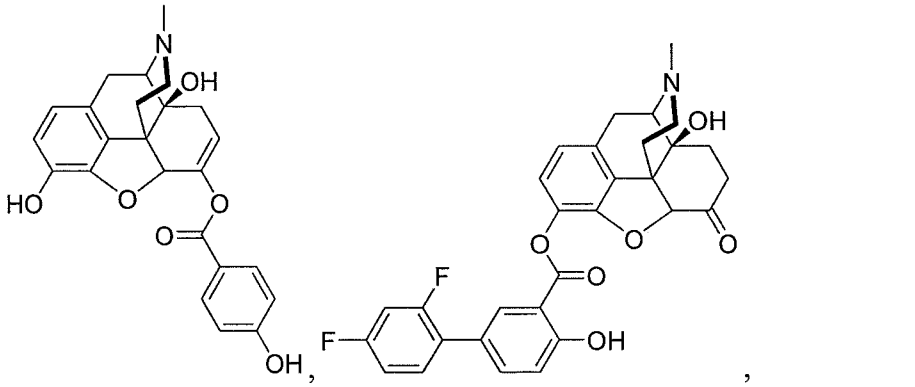
[0039] Figure 6 provides chemical structures of phenylproprionates for use in the making of conjugates of the present technology.

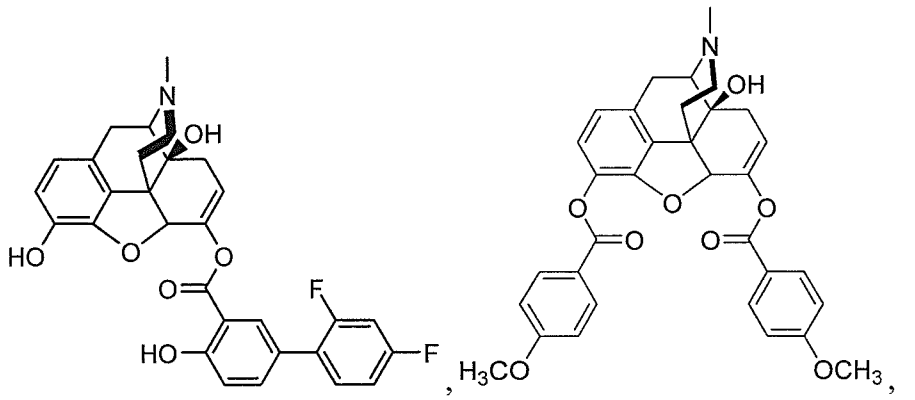
[0040] Figure 7 provides chemical structures of cinnamates for use in the making of conjugates of the present technology.

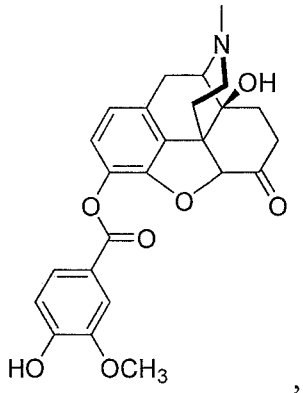
CLAIMS

1. A compound selected from the group consisting of









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and salts thereof.

2. A composition comprising at least one compound of claim 1, a salt thereof, or a combination thereof.

3. The composition of claim 2, wherein the composition is in a dosage form selected from the group consisting of: a tablet, a capsule, a caplet, a soft gel, a suppository, a troche, a lozenge, an oral powder, a solution, an oral film, a thin strip, a slurry, and a suspension.

4. The composition of claim 2, wherein the composition has reduced side effects when compared with unconjugated oxymorphone.

5. The composition of claim 4, wherein the reduced side effects comprise reduced opioid induced constipation.

6. The composition of claim 2, wherein the composition is in an amount sufficient to provide a therapeutically equivalent AUC when compared to an equivalent molar amount of unconjugated oxymorphone when administered orally.

7. The composition of claim 2, wherein the composition is in an amount sufficient to provide a therapeutically equivalent AUC and Cmax when compared to an equivalent molar amount of unconjugated oxymorphone when administered orally.

8. The composition of claim 2, wherein the composition is in an amount sufficient to provide a therapeutically equivalent AUC and a lower Cmax when compared to an equivalent molar amount of unconjugated oxymorphone when administered orally.

9. The composition of claim 2, wherein intranasal or intravenous administration of the at least one compound or salt thereof provides a lower AUC and/or Cmax when compared to an equivalent molar amount of unconjugated oxymorphone.

10. The composition of claim 2, wherein oral administration of the at least one compound or salt thereof provides a decreased overdose potential when compared to an equivalent molar amount of unconjugated oxymorphone.

11. The composition of claim 2, wherein the at least one compound or salt thereof provides an increased tamper resistance when compared to an equivalent molar amount of unconjugated oxymorphone.

12. The composition of claim 2, wherein the salt of the compound is a pharmaceutically acceptable anionic or cationic salt form or salt mixture thereof.

13. The composition of claim 12, wherein the anionic salt form is selected from the group consisting of an acetate, L-aspartate, besylate, bicarbonate, carbonate, D-camsylate, Lcamsylate, citrate, edisylate, formate, fumarate, gluconate, hydrobromide/bromide, hydrochloride/chloride, D-lactate, L-lactate, D,L-lactate, D,L-malate, L-malate, mesylate, pamoate, phosphate, succinate, sulfate, bisulfate, D-tartrate, L-tartrate, D,L-tartrate, mesotartrate, benzoate, gluceptate, D-glucuronate, hybenzate, isethionate, malonate, methylsulfate, 2-napsylate, nicotinate, nitrate, orotate, stearate, tosylate, thiocyanate, acefyllinate, aceturate, aminosalicylate, ascorbate, borate, butyrate, camphorate, camphocarbonate, decanoate, hexanoate, cholate, cypionate, dichloroacetate, edentate, ethyl sulfate, furate, fusidate, galactarate, galacturonate, gallate, gentisate, glutamate, glutarate, glycerophosphate, heptanoate, hydroxybenzoate, hippurate, phenylpropionate, iodide, xinafoate, lactobionate, laurate, maleate, mandelate, methanesulfonate, myristate, napadisilate, oleate, oxalate, palmitate, picrate, pivalate, propionate, pyrophosphate, salicylate, salicylsulfate, sulfosalicylate, tannate, terephthalate, thiosalicylate, tribrophenate, valerate, valproate, adipate, 4-acetamidobenzoate, camsylate, octanoate, estolate, esylate, glycolate, thiocyanate, and undecylenate or a mixture thereof.

14. The composition of claim 12, wherein the cationic salt form is selected from the group consisting of sodium, potassium, calcium, magnesium, zinc, aluminum, lithium, cholinate, lysinium, ammonium, or tromethamine.

15. The composition of claim 2, wherein the compound is present in an amount per unit dose of between 1 mg and 100 mg per unit dose wherein the amount per unit dose is based on the content of oxymorphone.

16. The composition of claim 2, wherein the composition is formulated for oral administration, suppository administration, or powder for injection.

17. The composition of claim 16, wherein the composition formulated for oral administration is a tablet, a capsule, a soft gel, a caplet, a pill, an oral powder, a troche, a lozenge, a slurry, a solution, a suspension, an emulsion, or an oral thin film (OTF).

18. The composition of claim 17, wherein the composition is formulated in a tablet form, a solution, a suspension, or a soft gel form.

19. The composition of claim 18, wherein the tablet form further comprises one or more excipients, wherein the excipients are selected from the group consisting of anti-adherents, binders, coatings, disintegrants, fillers, flavors, dyes, colors, glidants, lubricants, preservatives, sorbents, sweeteners, derivatives thereof, and combinations thereof.

20. The composition of claim 19, wherein the binder is selected from the group consisting of hydroxypropylmethylcellulose, ethyl cellulose, povidone, acrylic and methacrylic acid copolymers, pharmaceutical glaze, gums, and milk derivatives.

21. The composition of claim 2, wherein the compound exhibits an improved AUC and rate of release over time when compared to an equivalent molar amount of unconjugated oxymorphone over the same time period when administered orally.

22. The composition of claim 2, wherein the compound exhibits less variability in the oral PK profile when compared to an equivalent molar amount unconjugated oxymorphone.