CLAIMS

1. An acetate salt of buprenorphine comprising a tetrahydrate.

2. A purified acetate salt of buprenorphine of claim 1.

3. The purified acetate salt of buprenorphine of claim 2, which is an essentially pure acetate salt of buprenorphine.

4. A crystalline form of the acetate salt of buprenorphine of any one of claims 1 to 3.

5. The crystalline form of claim 4, characterized by an X-ray powder diffraction pattern obtained by exposure to CuKα radiation comprising peaks at 2Θ angles substantially equivalent to at least the peaks at 16.21 and 18.70, and having at least one additional peak at a 2Θ angle substantially equivalent to at least one of the peaks at 8.77, 10.31, or 18.47.

6. A method for preparing an acetate salt of buprenorphine, comprising the steps of:

(a) contacting buprenorphine free base with a solution comprising acetic acid in a dissolution vessel to form an admixture, wherein the admixture is at a temperature of from about 40 °C to about 80 °C;

(b) optionally filtering the admixture of step (a);

(c) adding an agent to the admixture produced in step (a) or (b) to precipitate the acetate salt of buprenorphine; and

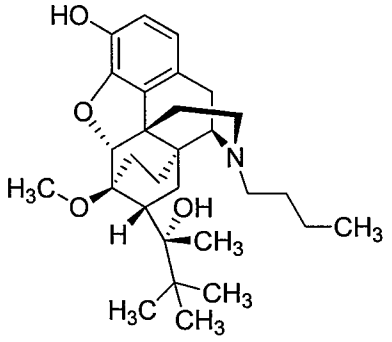
(d) isolating the acetate salt of buprenorphine precipitated in step (c).

7. The method of claim 6, wherein in step (c) the agent is selected from an anti-solvent, a seed crystal, and combinations thereof.

8. The method of claim 6 or claim 7, further comprising cooling the admixture to a temperature of about 30 °C or lower following addition of the agent and prior to isolating the acetate salt of buprenorphine in step (d).

9. A buprenorphine acetate salt product obtained from the method of any one of claims 6-8.

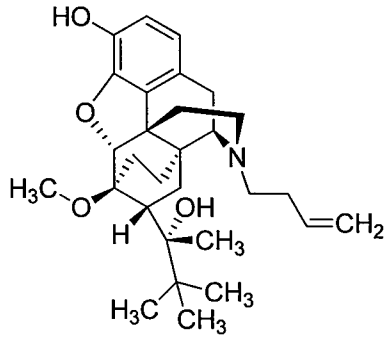
10. The product of claim 9, wherein the product comprises about 0.10 wt% or less of a compound of formula (12):



(12)

or a salt thereof.

11. The product of claim 9 or claim 10, wherein the product comprises about 0.10 wt% or less of a compound of formula (13):



(13)

or a salt thereof.

12. A method for preparing buprenorphine free base comprising the steps of:

(a) contacting an acetate salt of buprenorphine with a solution and a basic material to form an admixture;

(b) agitating the admixture of step (a) at a temperature of from about 20 °C to about 90 °C to provide buprenorphine free base;

(c) isolating the buprenorphine free base of step (b); and

(d) optionally repeating steps (a) through (c) one or more times.

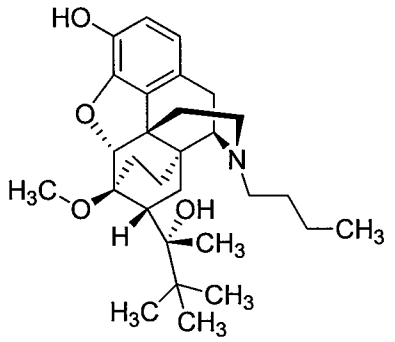
13. The method of claim 12, wherein the solution of step (a) comprises water and an alcohol.

14. The method of claim 12 or claim 13, wherein the alcohol is selected from methanol, ethanol, isopropyl alcohol, and combinations thereof.

15. The method of claim 12, wherein the basic material is selected from a hydroxide, carbonate, alkoxide, hydride, phosphate, borate, oxide, cyanide, silicate, amine, and combinations thereof.

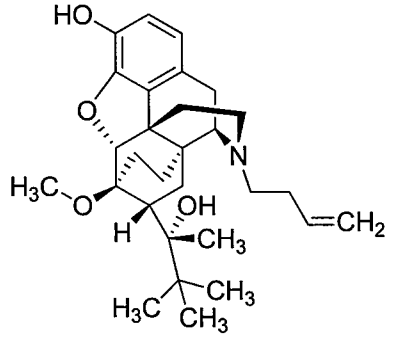
16. A buprenorphine free base product obtained from the method of any one of claims 12-15.

17. The product of claim 16, wherein the product comprises about 0.10 wt% or less of a compound of formula (12):



(12) .

18. The product of claim 16 or claim 17, wherein the product comprises about 0.10 wt% or less of a compound of formula (13):



(13) .

19. A pharmaceutical composition comprising the product of any one of claims 16-18 and a pharmaceutically acceptable carrier.

20. A method for preparing buprenorphine free base, comprising placing an acetate salt of buprenorphine under a pressure and temperature for a time sufficient to remove the acetic acid by evaporating under atmospheric pressure or sub-atmospheric pressure.

21. The method of claim 20, wherein the pressure is a sub-atmospheric pressure of from about 100 Torr to about 200 Torr.

22. The method of claim 21, wherein the temperature is at least about 30 °C and the time is at least about 1 hour.

23. A method for preparing buprenorphine free base, comprising the steps of:

(a) dissolving an acetate salt of buprenorphine in a solution to form an admixture;

(b) optionally filtering the admixture of step (a);

(c) adding a basic material to the admixture in step (a) or (b) to form a second admixture;

(d) adding an anti-solvent to the second admixture produced in step (c) to form a precipitate of the buprenorphine free base; and

(e) isolating the precipitate from step (d).

24. A method for preparing buprenorphine free base comprising:

(a) heating an admixture of an acetate salt of buprenorphine and an aqueous solution to provide precipitated buprenorphine free base; and

(b) filtering the admixture of step (a).

25. A method for preparing buprenorphine free base: comprising:

(a) mixing an acetate salt of buprenorphine in a solvent to form an admixture;

(b) refluxing the admixture at a reflux temperature and removing the acetate as acetic acid in the vapor phase;

(c) cooling the admixture to provide precipitated buprenorphine free base; and

(d) isolating the buprenorphine free base.

26. A buprenorphine free base product obtained from the method of claim 24 or claim 25.

27. A pharmaceutical composition comprising the acetate salt of buprenorphine of any one of claims 1-3 or the crystalline form of claim 4 or claim 5 or the product of any one of claims 9-11 or 26 and a pharmaceutically acceptable carrier.

28. Use of a product of any one of claims 9-11, 16-18 and 26 or the pharmaceutical composition of claim 19 or claim 27 or an acetate salt of buprenorphine of any one of claim 1 to 3 or the crystalline form of an acetate salt of buprenorphine of claim 4 or claim 5 in the manufacture of a medicament for the treatment of pain.

29. Product of any one of claims 9-11, 16-18 and 26 or the pharmaceutical composition of claim 19 or claim 27 or an acetate salt of buprenorphine of any one of claim 1 to 3 or the crystalline form of an acetate salt of buprenorphine of claim 4 or claim 5 for use in the treatment of pain.