CLAIMS

1. A composition comprises a plurality of multi-layer pellets comprising:
    a. a water soluble core;
    b. an antagonist containing layer comprising naltrexone HCl coating the core;
    c. a sequestering polymer layer coating the antagonist containing layer;
    d. an agonist layer comprising an opioid agonist coating the sequestering polymer layer; and
    e. a controlled release layer coating the agonist layer;

    wherein the naltrexone HCl comprises at least 10% wt to wt of the opioid agonist and wherein the agonist is substantially released and the naltrexone HCl is substantially sequestered upon administration to a human being.

2. The composition of claim 1 wherein the naltrexone HCl comprises from about 10% to about 30% wt to wt of the opioid agonist.

3. The composition of claim 1 wherein the naltrexone HCl comprises from about 10% to about 25% wt to wt of the opioid agonist.

4. The composition of claim 1 wherein the naltrexone HCl comprises from about 10% to about 20% wt to wt of the opioid agonist.

5. The composition of claim 1 wherein the opioid agonist is oxycodone.

6. A composition comprises a plurality of multi-layer pellets comprising:
    a. a water soluble core;
    b. an antagonist containing layer comprising naltrexone HCl coating the core;
    c. a sequestering polymer layer coating the antagonist containing layer;
    d. an agonist layer comprising an opioid agonist coating the sequestering polymer layer; and
    e. a controlled release layer coating the agonist layer;

    wherein the weight of the naltrexone HCl comprises at least 5% the combined weight of the water soluble core, antagonist layer and sequestering polymer

layer and wherein the agonist is substantially released and the naltrexone HCl is substantially sequestered upon administration to a human being.

7. The composition of claim 6 wherein the weight of the naltrexone HCl comprises from about 5% to about 30% of the combined weight of the water soluble core, antagonist layer and sequestering polymer layer.

8. The composition of claim 6 wherein the weight of the naltrexone HCl comprises from about 6% to about 25% of the combined weight of the water soluble core, antagonist layer and sequestering polymer layer.

9. The composition of claim 6 wherein the weight of the naltrexone HCl comprises from about 7% to about 15% of the combined weight of the water soluble core, antagonist layer and sequestering polymer layer.

10. The composition of claim 6 wherein the weight of the naltrexone HCl comprises from about 8% to about 10% of the combined weight of the water soluble core, antagonist layer and sequestering polymer layer.

11. The composition of claim 6 wherein the opioid agonist is oxycodone.

12. A dosage form comprising oxycodone hydrochloride and sequestered naltrexone hydrochloride wherein the naltrexone hydrochloride is present in an amount that is about 10% to about 30% of amount of oxycodone hydrochloride on a weight basis wherein the dosage form sequesters 100% of the naltrexone hydrochloride as determined at 73 hours by first placing the composition in 500ml of a 0.1N HCl solution for 1 hour at 37°C, using USP paddle method, 100 rotations per minute, and then placing the composition in 500mL of a pH 7.5, 0.05M phosphate buffer for 72 hours at 37°C, using USP paddle method, 100 rotations per minute and then determining the amount of naltrexone hydrochloride sequestered.

13. The dosage form of claim 12 wherein the naltrexone hydrochloride is present in an amount that is about 12% the amount of oxycodone hydrochloride on a weight basis

14. The dosage form of claim 12 wherein the naltrexone hydrochloride is present in an amount that is about 12% the amount of oxycodone hydrochloride on a weight basis.

15. A composition comprising a plurality of multi-layer pellets comprising
    a. a water soluble core;
    b. an antagonist layer comprising naltrexone HCl coating the core;
    c. a sequestering polymer layer coating the antagonist containing layer;
    d. an agonist layer comprising an opioid agonist coating the sequestering polymer layer; and
    e. a controlled release layer coating the agonist layer

    wherein the naltrexone HCl comprises at least 10% wt to wt of the opioid agonist and wherein the agonist is substantially released with a time to maximum observed plasma concentration (T_{max}) is more than about 10 hours and the naltrexone HCl is substantially sequestered upon administration to a human being.

16. The composition of claim 15 wherein the T_{max} is more than about 12 hours.

17. The composition of claim 15 wherein the T_{max} is more than about 14 hours.

18. The composition of claim 15 wherein the T_{max} is from about 10 hours to about 16 hours.

19. The composition of claim 15 wherein the T_{max} is from about 12 hours to about 16 hours.

20. Use of a multi-layer pharmaceutical composition comprising:
    a. a water soluble core;
    b. an antagonist layer comprising naltrexone HCl coating the core;
    c. a sequestering polymer layer coating the antagonist containing layer;
    d. an agonist layer comprising an opioid agonist coating the sequestering polymer layer; and

e. a controlled release layer coating the agonist layer

in the manufacture of a medicament for the treatment of moderate to severe chronic pain in a patient in need thereof, wherein the naltrexone HCl comprises at least 10% wt to wt of the opioid agonist and wherein the agonist is substantially released with a time to maximum observed plasma concentration (T_{max}) is more than about 10 hours and the naltrexone HCl is substantially sequestered upon administration to a human being.

21. Use of a multi-layer pharmaceutical composition comprising:

a. a water soluble core;

b. an antagonist layer comprising naltrexone HCl coating the core;

c. a sequestering polymer layer coating the antagonist containing layer;

d. an agonist layer comprising an opioid agonist coating the sequestering polymer layer; and

e. a controlled release layer coating the agonist layer

in the manufacture of a medicament for the treatment of moderate to severe chronic pain in a patient in need thereof, wherein the naltrexone HCl comprises at least 10% wt to wt of the opioid agonist and wherein the agonist is substantially released with a ratio of plasma concentration of the agonist at 24 hours after administration (C_{24}) to maximum observed plasma concentration (C_{max}) of between about 0.2 to about 0.8.

CLAIMS

1. A composition comprises a plurality of multi-layer pellets comprising:
   a. a water soluble core;
   b. an antagonist containing layer comprising naltrexone HCl coating the core;
   c. a sequestering polymer layer coating the antagonist containing layer;
   d. an agonist layer comprising an opioid agonist coating the sequestering polymer layer; and
   e. a controlled release layer coating the agonist layer;

wherein the weight of the naltrexone HCl comprises at least 5% the combined weight of the water soluble core, antagonist layer and sequestering polymer layer and wherein the agonist is substantially released and the naltrexone HCl is substantially sequestered upon administration to a human being.

2. The composition of claim 1, wherein the weight of the naltrexone HCl comprises from about 5% to about 30% of the combined weight of the water soluble core, antagonist layer and sequestering polymer layer.

3. The composition of claim 1, wherein the weight of the naltrexone HCl comprises from about 6% to about 25% of the combined weight of the water soluble core, antagonist layer and sequestering polymer layer.

4. The composition of claim 1, wherein the weight of the naltrexone HCl comprises from about 7% to about 15% of the combined weight of the water soluble core, antagonist layer and sequestering polymer layer.

5. The composition of claim 1, wherein the weight of the naltrexone HCl comprises from about 8% to about 10% of the combined weight of the water soluble core, antagonist layer and sequestering polymer layer.

6. The composition of claim 1, wherein the opioid agonist is oxycodone.

7. The composition of claim 1, wherein the naltrexone HCl comprises at least 10% wt to wt of the opioid agonist.

8. The composition of claim 7, wherein the naltrexone HCl comprises from about 10% to about 30% wt to wt of the opioid agonist.

9. The composition of claim 7, wherein the naltrexone HCl comprises from about 10% to about 25% wt to wt of the opioid agonist.

10. The composition of claim 7, wherein the naltrexone HCl comprises from about 10% to about 20% wt to wt of the opioid agonist.

11. The composition of claim 7, wherein the opioid agonist is oxycodone.

12. A dosage form comprising oxycodone hydrochloride and sequestered naltrexone hydrochloride wherein the naltrexone hydrochloride is present in an amount that is about 10% to about 30% of amount of oxycodone hydrochloride on a weight basis wherein the dosage form sequesters 100% of the naltrexone hydrochloride as determined at 73 hours by first placing the composition in 500ml of a 0.1N HCl solution for 1 hour at 37°C, using USP paddle method, 100 rotations per minute, and then placing the composition in 500mL of a pH 7.5, 0.05M phosphate buffer for 72 hours at 37°C, using USP paddle method, 100 rotations per minute and then determining the amount of naltrexone hydrochloride sequestered.

13. The dosage form of claim 12, wherein the naltrexone hydrochloride is present in an amount that is about 12% the amount of oxycodone hydrochloride on a weight basis.

14. A composition comprising a plurality of multi-layer pellets comprising

a. a water soluble core;
b. an antagonist layer comprising naltrexone HCl coating the core;
c. a sequestering polymer layer coating the antagonist containing layer;
d. an agonist layer comprising an opioid agonist coating the sequestering polymer layer; and
e. a controlled release layer coating the agonist layer

wherein the naltrexone HCl comprises at least 10% wt to wt of the opioid agonist

and wherein the agonist is substantially released with a time to maximum observed plasma concentration (T_{max}) is more than about 10 hours and the naltrexone HCl is substantially sequestered upon administration to a human being and wherein the weight of the naltrexone HCl comprises at least 5% the combined weight of the water soluble core, antagonist layer and sequestering polymer layer.

15. The composition of claim 14, wherein the T_{max} is more than about 12 hours.

16. The composition of claim 14, wherein the T_{max} is more than about 14 hours.

17. The composition of claim 14, wherein the T_{max} is from about 10 hours to about 16 hours.

18. The composition of claim 14, wherein the T_{max} is from about 12 hours to about 16 hours.

19. Use of a multi-layer pharmaceutical composition comprising:

a. a water soluble core;
b. an antagonist layer comprising naltrexone HCl coating the core;
c. a sequestering polymer layer coating the antagonist containing layer;
d. an agonist layer comprising an opioid agonist coating the sequestering polymer layer; and
e. a controlled release layer coating the agonist layer

in the manufacture of a medicament for the treatment of moderate to severe chronic pain in a patient in need thereof, wherein the naltrexone HCl comprises at least 10% wt to wt of the opioid agonist and wherein the agonist is substantially released with a time to maximum observed plasma concentration (T_{max}) is more than about 10 hours and the naltrexone HCl is substantially sequestered upon administration to a human being and wherein the weight of the naltrexone HCl comprises at least 5% the combined weight of the water soluble core, antagonist layer and sequestering polymer layer.

20. Use of a multi-layer pharmaceutical composition comprising:

a. a water soluble core;

b. an antagonist layer comprising naltrexone HCl coating the core;

c. a sequestering polymer layer coating the antagonist containing layer;

d. an agonist layer comprising an opioid agonist coating the sequestering polymer layer; and

d. a controlled release layer coating the agonist layer;

in the manufacture of a medicament for the treatment of moderate to severe chronic pain in a patient in need thereof, wherein the naltrexone HCl comprises at least 10% wt to wt of the opioid agonist and wherein the agonist is substantially released with a ratio of plasma concentration of the agonist at 24 hours after administration (C_{24}) to maximum observed plasma concentration (C_{max}) of between about 0.2 to about 0.8 and wherein the weight of the naltrexone HCl comprises at least 5% the combined weight of the water soluble core, antagonist layer and sequestering polymer layer.