aqueous or alcoholic solvent.

International application WO03/013479 thus describes the association of an opium-containing analgesic with its antagonist which significantly blocks the euphoric effect of the opioid analgesic. Both compounds are released at the same time. However, this type of pharmaceutical formulation comprising an opium-containing agonist and its antagonist has drawbacks. In reality, the use of a pharmacologically active antagonist may be the cause of various problems.

Application EP 1 293 209 describes a modified release form using an ion exchange resin which limits extraction by chewing or use by inhalation or injection. However, this type of formulation does not prevent extraction using solvents or crushing.

International application WO2005/079760 describes a multi-particulate formulation using a plastic polymer (Eudragit® NE30D) which, because of its plastic properties and the concomitant use of a plasticizer, makes it difficult to crush said formulation. However, no provision is made with this formulation to prevent extraction by solvent.

At present, sustained release formulations therefore exist which use different galenic ploys to obtain this modified release, but none of the systems described can guard against the illegal extraction of the active ingredient. Such a formulation therefore needs to be developed.

SUMMARY

In a first aspect, there is provided a granule comprising a solid core on which an active ingredient is supported, said granule also comprising, supported on said solid core, the following compounds:

-one or more colouring agents,

-one or more metallic pigments,

-one or more gas-releasing compounds,

-and optionally one or more embittering agents.

In a second aspect, there is provided a pharmaceutical compound comprising granules as defined herein.

In a third aspect, there is provided a process of preparing a granule as defined herein, comprising a step of applying the active ingredient to the insoluble support by powdering.

DETAILED DESCRIPTION

An object of the present invention is therefore to provide pharmaceutical formulations specifically designed to prevent the inappropriate use of medicinal drugs.

An object of the present invention is to provide pharmaceutical formulations to guard against illicit extraction of the active ingredient.

An object of the present invention is to provide medicinal compounds, particularly oral compounds, specially formulated to provide greater security against the problems of inappropriate use of medicinal drugs.

An object of the present invention is to provide pharmaceutical formulations that remedy and add to existing devices in order to reduce and render impossible the inappropriate use of

Claims

1. Granule comprising a solid core on which an active ingredient is supported, said core being chosen preferably from insoluble supports, and more particularly from the group of polyols, gums, silicone derivatives, derivatives of calcium or potassium, mineral compounds such as dicalcic phosphates, tricalcic phosphates and calcium carbonates, saccharose, cellulose derivatives, particularly microcrystalline cellulose, ethyl cellulose and hydroxypropyl methyl cellulose, starch and mixtures thereof,
said granule also comprising, supported on said solid core, the following compounds:

- one or more colouring agents,

- one or more metallic pigments,

- one or more gas-releasing compounds,

- and optionally one or more embittering agents.

2. Granule according to claim 1, characterised in that the gas-releasing compound is chosen from the group of carbonates and bicarbonates, and in particular is chosen from the group of sodium bicarbonate, sodium carbonate, sodium glycine carbonate, potassium bicarbonate, magnesium carbonate and calcium carbonate.

3. Granule according to either claim 1 or claim 2, in which the metallic pigments are titanium dioxide-based pigments present on the surface of said granule.

4. Granule according to any one of claims 1 to 3, characterised in that the active ingredient is chosen from the group of antalgics and analgesics.

5. Granule according to any one of claims 1 to 4, characterised in that the active ingredient is chosen from the group of morphine sulphate, oxycodone, gamma-hydroxybutyric acid or one of its salts, buprenorphine, modafinil, dextropropoxyphene, methadone, tramadol, nalbuphine, tetrahydrocannabinol and benzodiazepines.

6. Granule according to any one of claims 1 to 5, characterised in that the embittering agent is chosen from the group of denatonium benzoate, extracts of gentian, quinine, caffeine, brucine, quassin, propylthiouracil (PROP), phenylthiocarbamide (PTC), astringent compounds such as tannins, grapefruit flavour and bitter cocoa flavour.

7. Granule according to any one of claims 1 to 6, characterised in that it comprises from 0.5 % to 60 % by weight of active ingredient in relation to the total weight of the granule.

8. Granule according to any one of claims 1 to 7, characterised in that it comprises from 0.2 % to 4 % by weight of colouring agent, from 0.1 % to 5 % by weight of metallic pigments and from 5 % to 20 % by weight of gas-releasing compounds in relation to the total weight of the granule.

9. Granule according to any one of claims 1 to 8, characterised in that the solid core represents from 10 % to 85 % by weight in relation to the total weight of the granule.

10. Pharmaceutical compound comprising granules according to any one of claims 1 to 9.

11. Process of preparing a granule according to any one of claims 1 to 9, characterised in that it comprises a step of applying the active ingredient to the insoluble support by powdering.

12. Process according to claim 11, in which the active ingredient is mixed with the colouring agents, metallic pigments and gas-releasing compounds before the step of applying to the insoluble support by powdering.

Claims

1. Granule comprising a solid core on which an active ingredient is supported, said granule also comprising, supported on said solid core, the following compounds:

   -one or more colouring agents,
   -one or more metallic pigments,
   -one or more gas-releasing compounds,
   -and optionally one or more embittering agents.

2. Granule according to claim 1, wherein the core is chosen from insoluble supports.

3. Granule according to claim 2, wherein the core is chosen from the group of polyols, gums, silicone derivatives, derivatives of calcium or potassium, mineral compounds such as dicalcic phosphates, tricalcic phosphates and calcium carbonates, saccharose, cellulose derivatives, starch and mixtures thereof.

4. Granule according to claim 3, wherein the core is chosen from microcrystalline cellulose, ethyl cellulose and hydroxypropyl methyl cellulose, and mixtures thereof.

5. Granule according to any one of claims 1 to 4, wherein the gas-releasing compound is chosen from the group of carbonates and bicarbonates.

6. Granule according to claim 5, wherein the gas-releasing compound is chosen from the group of sodium bicarbonate, sodium carbonate, sodium glycine carbonate, potassium bicarbonate, magnesium carbonate and calcium carbonate.

7. Granule according to any one of claims 1 to 6, in which the metallic pigments are titanium dioxide-based pigments present on the surface of said granule.

8. Granule according to any one of claims 1 to 7, wherein the active ingredient is chosen from the group of antalgics and analgesics.

9. Granule according to any one of claims 1 to 8, wherein the active ingredient is chosen from the group of morphine sulphate, oxycodone, gamma-hydroxybutyric acid or one of its salts, buprenorphine, modafinil, dextropropoxyphene, methadone, tramadol, nalbuphine, tetrahydrocannabinol and benzodiazepines.

10. Granule according to any one of claims 1 to 9, wherein the embittering agent is chosen from the group of denatonium benzoate, extracts of gentian, quinine, caffeine, brucine, quassin, propylthiouracil (PROP), phenylthiocarbamide (PTC), astringent compounds such as tannins, grapefruit flavour and bitter cocoa flavour.

11. Granule according to any one of claims 1 to 10, comprising from 0.5 % to 60 % by weight of active ingredient in relation to the total weight of the granule.

12. Granule according to any one of claims 1 to 11, comprising from 0.2 % to 4 % by 5 weight of colouring agent, from 0.1 % to 5 % by weight of metallic pigments and from 5 % to 20 % by weight of gas-releasing compounds in relation to the total weight of the granule.

13. Granule according to any one of claims 1 to 12, wherein the solid core represents from 10 % to 85 % by weight in relation to the total weight of the granule.

14. Pharmaceutical compound comprising granules according to any one of claims 1 to 13.

15. Process of preparing a granule according to any one of claims 1 to 13, comprising a step of applying the active ingredient to the insoluble support by powdering.

16. Process according to claim 15, in which the active ingredient is mixed with the colouring agents, metallic pigments and gas-releasing compounds before the step of applying to the insoluble support by powdering.