The process for manufacturing the novel dosage form according to the present invention generally comprises the following steps:

(a) providing quetiapine or a pharmaceutically acceptable salt thereof,

(b) adding to the quetiapine or to the mixture obtained in step (a) a hydrophobic controlled release agent or sodium starch glycolate, and at least one diluent and a pH dependent polymer; and

(c) adding a solvent mixture, comprising a binder to the mixture obtained step (b);

(d) wet granulating the mixture obtained in step (c);

(e) drying the granules in step (d); and

(f) sieving the dried granules with a lubricant; and

(g) blending the granules of step (f) with extragranular excipients in a suitable non shear blender;

(h) compressing the blend of step (g) into a tableted dosage form; and

(~~h~~i) optionally coating the granules/tablets with an aqueous dispersion.

Preferably, the at least one hydrophobic controlled release agent is stearic acid or Cutina® HR PH (i.e. hydrogenated castor oil). Preferably, the pH dependent polymer is Eudragit® (i.e. a methacrylic acid copolymer), and more preferably, the pH dependent polymer is selected from Eudragit L 30 D-55, Eudragit L100-55, and mixtures thereof. For the avoidance of doubt, Eudragit L 30 D-55 and Eudragit L100-55 are both poly(methacrylic acid-co-ethyl acrylate) 1:1 - see the following web pages: http://eudragit.evonik.com/product/eudragit/en/products-services/eudragit-products/enteric-formulations/l-30-d-55/pages/default.aspx & http://eudragit.evonik.com/product/eudragit/en/products-services/eudragit-products/enteric-formulations/l-100-55/pages/default.aspx

It is to be understood that while the invention has been described in conjunction with the preferred specific embodiments thereof, that the description above as well as the examples which follow are intended to illustrate and not limit the scope of the invention. Other aspects, advantages and modifications within the scope of the invention will be apparent to those skilled in the art to which the invention pertains. Although any method and material whether similar or equivalent to those described herein can be used in the practice for testing the present invention, the preferred methods and materials as described.

CLAIMS

1. A novel stable controlled release pharmaceutical dosage form comprising:
   - intragranular excipients comprising:
     - quetiapine or a pharmaceutically acceptable salt thereof;
     - at least one hydrophobic controlled release agent,
     - at least one pH dependent polymer; and
   - extragranular excipients comprising at least one pharmaceutically acceptable excipient.

2. The novel controlled release pharmaceutical dosage form according to claim 1, wherein the content (in % by weight) of the at least one hydrophobic controlled release agent is in the range of about 4.5% to about 35% and the content of the at least one pH dependent polymer is in the range of about 15% to about 35%.

3. The novel controlled release pharmaceutical dosage form according to claim 1 or 2, wherein the ratio of the % by weight content between the at least one hydrophobic controlled release agent and the at least one pH dependent polymer ranges from about 1:3 to about 1:7.

4. The novel controlled release pharmaceutical dosage form according to claim 1 or 2, wherein the ratio of the % by weight content between the at least one hydrophobic controlled release agent and the at least one pH dependent polymer ranges from about 1:4 to about 1:6.

5. The novel controlled release pharmaceutical dosage form according to claim 1 or 2, wherein the ratio of the % by weight content between the at least one hydrophobic controlled release agent and the at least one pH dependent polymer ranges from about 1:4.5 to about 1:5.5.

6. The novel controlled release pharmaceutical dosage form according to any one of claims 1 to 5, wherein the at least one hydrophobic controlled release agent is stearic acid.

7. The novel controlled release pharmaceutical dosage form according to any one of claims 1 to 5, wherein the at least one hydrophobic controlled release agent is an hydrogenated castor oil.

8. The novel controlled release pharmaceutical dosage form according to any one of claims 1 to 7, wherein the pH dependent polymer is a methacrylic acid copolymer.

9. The novel controlled release pharmaceutical dosage form according to claim 8, wherein the pH dependent polymer is Eudragit.

10. The novel controlled release pharmaceutical dosage form according to claim 9, wherein the pH dependent polymer is selected from Eudragit L 30 D-55, Eudragit L100-55, and mixtures thereof.

11. The novel stable controlled release pharmaceutical dosage form according to any one of claims 1 to 10, wherein said dosage form provides a dissolution of quetiapine or pharmaceutically acceptable salt thereof between about 30 and about 45 % within 1 hour, between about 45 and about 70 % within 6 hours and between about 75 % and about 95 % within 16 hours as measured by Apparatus I USP (baskets) at 100 rpm, in 1000mL of 0.1N HCl (1.2 pH) for the first hour, in 1000mL of 4.5 pH acetate buffer for the 2 hour and subsequently in 1000mL of 6.8 pH phosphate buffer.

12. The novel stable controlled release pharmaceutical dosage form according to any one of claims 1 to 10, wherein said dosage form provides a dissolution of quetiapine or pharmaceutically acceptable salt thereof between about 50% and about 60% (by wt) of quetiapine or pharmaceutically acceptable salt thereof released after 2 hours; between about 60% and about 70% (by wt) after 4 hours; between about 65% and about 80% (by wt) of quetiapine or pharmaceutically acceptable salt thereof released after 8 hours; between about 70% and between 80% (by wt) of quetiapine or pharmaceutically

acceptable salt thereof released after 12 hours; and over about 75% (by wt) of quetiapine or pharmaceutically acceptable salt thereof released after 16 hours, as measured by USP Basket (Apparatus I) Method at 200 rpm at 1000 ml aqueous buffer pH 1.2 from 0 to 2 hours and pH 6.8 from 4 to 20 hours at 37°C.

CLAIMS

1. A novel stable controlled release pharmaceutical dosage form comprising:
   - intragranular excipients comprising:
     - quetiapine or a pharmaceutically acceptable salt thereof;
     - at least one hydrophobic controlled release agent,
     - at least one pH dependent polymer; and
   - extragranular excipients comprising at least one pharmaceutically acceptable excipient.

2. The novel controlled release pharmaceutical dosage form according to claim 1, wherein the content (in % by weight) of the at least one hydrophobic controlled release agent is in the range of about 4.5% to about 35% and the content of the at least one pH dependent polymer is in the range of about 15% to about 35%.

3. The novel controlled release pharmaceutical dosage form according to claim 1 or 2, wherein the ratio of the % by weight content between the at least one hydrophobic controlled release agent and the at least one pH dependent polymer ranges from about 1:3 to about 1:7.

4. The novel controlled release pharmaceutical dosage form according to claim 1 or 2, wherein the ratio of the % by weight content between the at least one hydrophobic controlled release agent and the at least one pH dependent polymer ranges from about 1:4 to about 1:6.

5. The novel controlled release pharmaceutical dosage form according to claim 1 or 2, wherein the ratio of the % by weight content between the at least one hydrophobic controlled release agent and the at least one pH dependent polymer ranges from about 1:4.5 to about 1:5.5.

6. The novel controlled release pharmaceutical dosage form according to any one of claims 1 to 5, wherein the at least one hydrophobic controlled release agent is stearic acid.

7. The novel controlled release pharmaceutical dosage form according to any one of claims 1 to 5, wherein the at least one hydrophobic controlled release agent is an hydrogenated castor oil.

8. The novel controlled release pharmaceutical dosage form according to any one of claims 1 to 7, wherein the pH dependent polymer is a methacrylic acid copolymer.

9. The novel controlled release pharmaceutical dosage form according to claim 8, wherein the pH dependent polymer is Poly(methacylic acid-co-ethyl acrylate) 1:1.

10. The novel stable controlled release pharmaceutical dosage form according to any one of claims 1 to 9, wherein said dosage form provides a dissolution of quetiapine or pharmaceutically acceptable salt thereof between about 30 and about 45 % within 1 hour, between about 45 and about 70 % within 6 hours and between about 75 % and about 95 % within 16 hours as measured by Apparatus I USP (baskets) at 100 rpm, in 1000mL of 0.1N HCl (1.2 pH) for the first hour, in 1000mL of 4.5 pH acetate buffer for the 2 hour and subsequently in 1000mL of 6.8 pH phosphate buffer.

11. The novel stable controlled release pharmaceutical dosage form according to any one of claims 1 to 9, wherein said dosage form provides a dissolution of quetiapine or pharmaceutically acceptable salt thereof between about 50% and about 60% (by wt) of quetiapine or pharmaceutically acceptable salt thereof released after 2 hours; between about 60% and about 70% (by wt) after 4 hours; between about 65% and about 80% (by wt) of quetiapine or pharmaceutically acceptable salt thereof released after 8 hours; between about 70% and between 80% (by wt) of quetiapine or pharmaceutically acceptable salt thereof released after 12 hours; and over about 75% (by wt) of quetiapine or pharmaceutically acceptable salt thereof released after 16 hours, as measured by USP

Basket (Apparatus I) Method at 200 rpm at 1000 ml aqueous buffer pH 1.2 from 0 to 2 hours and pH 6.8 from 4 to 20 hours at 37°C.