penetrate into the modified release portion,
[12] the pharmaceutical composition for oral administration of [11], wherein the additive which allows water to penetrate into the modified release portion has a solubility such that the amount of water necessary to dissolve 1 g of the additive is 10 mL or less,
[13] the pharmaceutical composition for oral administration of [11] or [12], wherein the content of the additive which allows water to penetrate into the modified release portion is about 5% by weight to about 75% by weight with respect to the weight of the modified release portion,
[14] the pharmaceutical composition for oral administration of any one of [1] to [13], which is a pharmaceutical composition for treating urinary urgency, urinary frequency, and/or urge urinary incontinence associated with overactive bladder,
[15] the pharmaceutical composition for oral administration of any one of [1] to [14], wherein the pharmaceutical composition is a tablet,
[16] the pharmaceutical composition for oral administration of [15], which is a bi-layered tablet, and
[17] a pharmaceutical composition for oral administration comprising (1) a layer comprising mirabegron or a pharmaceutically acceptable salt thereof, and (2) a layer comprising solifenacin or a pharmaceutically acceptable salt thereof, and calcium stearate.

[18] Use of the pharmaceutical composition as disclosed herein, in the manufacture of a medicament for treating urinary urgency, urinary frequency, and/or urge urinary incontinence associated with overactive bladder.

[0017a] The present invention also provides a bi-layered pharmaceutical composition for oral administration comprising:

(1) a modified release layer comprising mirabegron or a pharmaceutically acceptable salt thereof, and

(2) an immediate release layer comprising solifenacin or a pharmaceutically acceptable salt thereof, and calcium stearate.

[0017b] The present invention also provides a pharmaceutical composition for oral administration comprising:
(1) a layer comprising mirabegron or a pharmaceutically acceptable salt thereof, and

(2) a layer comprising solifenacin or a pharmaceutically acceptable salt thereof, and calcium stearate.

[0017c] The present invention also provides a bi-layered pharmaceutical composition for oral administration comprising:

(1) a modified release layer comprising mirabegron or a pharmaceutically acceptable salt thereof and a polymer which forms a hydrogel, wherein the hydrogel-forming polymer has an average molecular weight of about 100,000 with a viscosity of 12 mPa·s to 50 mPa·s in a 5% aqueous solution at 25°C to about 5,000,000 with a viscosity of 5,500 mPa·s to 7500 mPa·s in a 1% aqueous solution at 25°C, and

(2) an immediate release layer comprising solifenacin or a pharmaceutically acceptable salt thereof, and calcium stearate.

ADVANTAGEOUS EFFECTS OF INVENTION

[0018]

The present invention provides a pharmaceutical composition for oral administration comprising a modified release portion containing mirabegron or a pharmaceutically acceptable salt thereof, and an immediate release portion containing solifenacin or a pharmaceutically acceptable salt thereof. The pharmaceutical composition for oral administration of the present invention has a drug release similar to that of each current formulation (single drug formulation), and thus, a single formulation (combined formulation) capable of expecting pharmacological effects

CLAIMS

1. A pharmaceutical composition for oral administration comprising:

(1) a modified release portion comprising mirabegron or a pharmaceutically acceptable salt thereof, and

(2) an immediate release portion comprising solifenacin or a pharmaceutically acceptable salt thereof, and calcium stearate.

2. The pharmaceutical composition for oral administration according to claim 1, wherein the immediate release portion is disintegrated and/or dissolved before the modified release portion forms a gel.

3. The pharmaceutical composition for oral administration according to claim 1 or 2, wherein about 85% or more of solifenacin is dissolved after 15 minutes.

4. The pharmaceutical composition for oral administration according to claim 3, wherein 90% or more of solifenacin is dissolved after 60 minutes.

5. The pharmaceutical composition for oral administration according to any one of claims 1 to 4, wherein the content of calcium stearate is about 0.1% by weight to about 10% by weight with respect to the weight of the immediate release portion.

6. The pharmaceutical composition for oral administration according to any one of claims 1 to 5, wherein the modified release portion contains a polymer which forms a hydrogel.

7. The pharmaceutical composition for oral administration according to claim 6, wherein the hydrogel-forming polymer has an average molecular weight of about 100,000 or more, or a viscosity of 12 mPa·s or more in a 5% aqueous solution at 25°C.

8. The pharmaceutical composition for oral administration according to claim 7, wherein the hydrogel-forming polymer is one polymer or two or more polymers selected from the group consisting of polyethylene oxide, hypromellose, hydroxypropylcellulose, methylcellulose, carboxymethylcellulose sodium, hydroxyethylcellulose, and a carboxyvinyl polymer.

9. The pharmaceutical composition for oral administration according to claim 8, wherein the hydrogel-forming polymer is polyethylene oxide.

10. The pharmaceutical composition for oral administration according to any one of claims 6 to 9, wherein the content of the hydrogel-forming polymer is about 1% by weight to about 70% by weight with respect to the weight of the modified release portion.

11. The pharmaceutical composition for oral administration according to any one of claims 1 to 10, wherein the modified release portion further contains an additive which allows water to penetrate into the modified release portion.

12. The pharmaceutical composition for oral administration according to claim 11, wherein the additive which allows water to penetrate into the modified release portion has a solubility such that the amount of water necessary to dissolve 1 g of the additive is 10 mL or less.

13. The pharmaceutical composition for oral administration according to claim 11 or 12, wherein the content of the additive which allows water to penetrate into the modified release portion is about 5% by weight to about 75% by weight with respect to the weight of the modified release portion.

associated with overactive bladder.

14. The pharmaceutical composition for oral administration according to any one of claims 1 to 13, wherein the pharmaceutical composition is a tablet.

15. The pharmaceutical composition for oral administration according to claim 14, which is a bi-layered tablet.

16. Use of the pharmaceutical composition according to any one of claims 1 to 15, in the manufacture of a medicament for treating urinary urgency, urinary frequency, and/or urge urinary incontinence associated with overactive bladder.

18. A pharmaceutical composition for oral administration comprising:

(1) a layer comprising mirabegron or a pharmaceutically acceptable salt thereof, and

(2) a layer comprising solifenacin or a pharmaceutically acceptable salt thereof, and calcium stearate.

Claims

1. A bi-layered pharmaceutical composition for oral administration comprising:

(1) a modified release layer comprising mirabegron or a pharmaceutically acceptable salt thereof, and

(2) an immediate release layer comprising solifenacin or a pharmaceutically acceptable salt thereof, and calcium stearate.

2. The pharmaceutical composition for oral administration according to claim 1, wherein the immediate release layer is disintegrated and/or dissolved before the modified release layer forms a gel.

3. The pharmaceutical composition for oral administration according to claim 1, wherein about 85% or more of solifenacin is dissolved after 15 minutes.

4. The pharmaceutical composition for oral administration according to claim 3, wherein 90% or more of solifenacin is dissolved after 60 minutes.

5. The pharmaceutical composition for oral administration according to claim 1, wherein the content of calcium stearate is about 0.1% by weight to about 10% by weight with respect to the weight of the immediate release layer.

6. The pharmaceutical composition for oral administration according to claim 1, wherein the modified release layer contains a polymer which forms a hydrogel.

7. The pharmaceutical composition for oral administration according to claim 6, wherein the hydrogel-forming polymer has an average molecular weight of about 100,000 or more, or a viscosity of 12 mPa·s or more in a 5% aqueous solution at 25°C.

8. The pharmaceutical composition for oral administration according to claim 7, wherein the hydrogel-forming polymer is one polymer or two or more polymers selected from the group consisting of polyethylene oxide, hypromellose, hydroxypropylcellulose, methylcellulose, carboxymethylcellulose sodium, hydroxyethylcellulose, and a carboxyvinyl polymer.

9. The pharmaceutical composition for oral administration according to claim 8, wherein the hydrogel-forming polymer is polyethylene oxide.

10. The pharmaceutical composition for oral administration according to claim 6, wherein the content of the hydrogel-forming polymer is about 1% by weight to about 70% by weight with respect to the weight of the modified release layer.

11. The pharmaceutical composition for oral administration according to claim 1, wherein the modified release layer further contains an additive which allows water to penetrate into the modified release layer.

12. The pharmaceutical composition for oral administration according to claim 11, wherein the additive which allows water to penetrate into the modified release layer has a solubility such that the amount of water necessary to dissolve 1 g of the additive is 10 mL or less.

13. The pharmaceutical composition for oral administration according to claim 11, wherein the content of

the additive which allows water to penetrate into the modified release layer is about 5% by weight to about 75% by weight with respect to the weight of the modified release layer.

14. The pharmaceutical composition for oral administration according to claim 1, which is a pharmaceutical composition for treating urinary urgency, urinary frequency, and/or urge urinary incontinence associated with overactive bladder.

15. A pharmaceutical composition for oral administration comprising:

(1) a layer comprising mirabegron or a pharmaceutically acceptable salt thereof, and

(2) a layer comprising solifenacin or a pharmaceutically acceptable salt thereof, and calcium stearate.

16. A bi-layered pharmaceutical composition for oral administration comprising:

(1) a modified release layer comprising mirabegron or a pharmaceutically acceptable salt thereof and a polymer which forms a hydrogel, wherein the hydrogel-forming polymer has an average molecular weight of about 100,000 with a viscosity of 12 mPa·s to 50 mPa·s in a 5% aqueous solution at 25°C to about 5,000,000 with a viscosity of 5,500 mPa·s to 7500 mPa·s in a 1% aqueous solution at 25°C, and

(2) an immediate release layer comprising solifenacin or a pharmaceutically acceptable salt thereof, and calcium stearate.