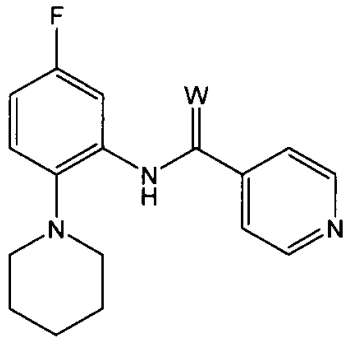
CLAIMS

1. A pharmaceutical composition for treating or preventing a disease caused in the vagina or perivaginal area by a pathogenic virus, the composition comprising, as an active ingredient, a compound selected from the group consisting of an aniline derivative represented by the following general formula (I):



(I)

wherein W represents S or O,
pharmaceutically acceptable salts thereof, and hydrates thereof,

the pharmaceutical composition being a pharmaceutical composition in the form of a vaginal insert (e.g., a vaginal tablet, a vaginal capsule or a vaginal suppository) containing a granular preparation,

the granular preparation comprising

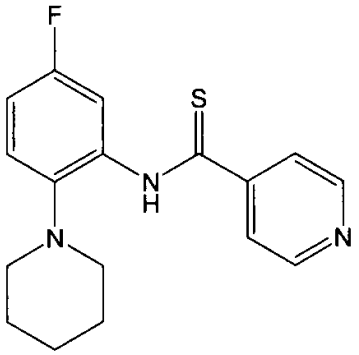
core particles containing the compound, needle-like and/or approximately column-like-shaped crystalline cellulose, a pharmaceutically acceptable approximately spherical shaped additive and a nonionic surfactant,

and a coating layer coating the core particles,

wherein the pharmaceutically acceptable approximately spherical shaped additive is lactose hydrate and/or corn starch, and the nonionic surfactant is polysorbate 80,

being characterized in that, in the core particles, voids are present between the crystalline cellulose and the additive.

2. The pharmaceutical composition according to claim 1, wherein the compound is a compound selected from the group consisting of an aniline derivative represented by the following formula (I-a):



(I－a)

, pharmaceutically acceptable salts thereof, and hydrates thereof.

3. The pharmaceutical composition according to claim 1 or 2, wherein at least part of the compound and at least part of the nonionic surfactant are retained in the voids of the core particles.

4. The pharmaceutical composition according to any one of claims 1 to 3, wherein the nonionic surfactant is contained in an amount of 2 times or less compared to the compound.

5. The pharmaceutical composition according to any one of claims 1 to 3, wherein the nonionic surfactant is contained in an amount of 1.5 times or less compared to the compound.

6. The pharmaceutical composition according to any one of claims 1 to 5, wherein the nonionic surfactant is contained in an amount of 1.5% by weight or more and less than 10% by weight with respect to the total amount of the pharmaceutical composition.

~~7. The pharmaceutical composition according to any one of claims 1 to 5, wherein the nonionic surfactant is contained in an amount of 7 to 8% by weight with respect to the total amount of the pharmaceutical composition.~~

~~8. The pharmaceutical composition according to any one of claims 1 to 3, wherein the nonionic surfactant is contained in an amount of 1.5% by weight or more and less than 10% by weight with respect to the total amount of the pharmaceutical composition and in an amount of 1.5 times or less compared to the compound.~~

~~9. The pharmaceutical composition according to any one of claims 1 to 8, wherein the nonionic surfactant is polysorbate.~~

7~~10~~. The pharmaceutical composition according to any one of claims 1 to 6~~9~~, wherein the pathogenic virus is human papillomavirus or herpes simplex virus.

8~~11~~. The pharmaceutical composition according to any one of claims 1 to 6~~9~~, wherein the disease is cervical

cancer or cervical intraepithelial neoplasia.

9~~12~~. The pharmaceutical composition according to claim 8~~11~~, wherein the disease is at least one disease selected from the group consisting of diseases diagnosed as LSIL, ASC-US, ASC-H, or HSIL according to the Bethesda classification, and diseases diagnosed as low-grade dysplastic cervical intraepithelial neoplasia (CIN1), moderate dysplastic cervical intraepithelial neoplasia (CIN2) or high-grade dysplastic cervical intraepithelial neoplasia (CIN3).

~~13. The pharmaceutical composition according to any one of claims 1 to 9, wherein the disease is condyloma acuminata.~~

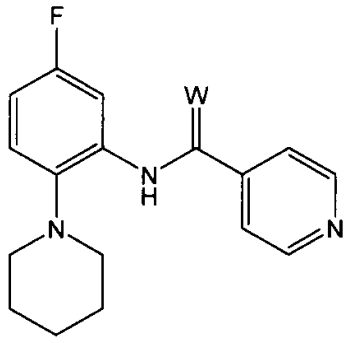
10~~14~~. The pharmaceutical composition according to any one of claims 1 to 9~~13~~, wherein the vaginal insert is in the form of a vaginal tablet.

11~~15~~. The pharmaceutical composition according to claim 10~~14~~, wherein vaginal tablet contains the compound in a dose of 10 mg to 50 mg.

12~~16~~. The pharmaceutical composition according to any one of claims 1 to 11~~15~~, wherein the compound is administered to the patient in a dose of 10 mg to 50 mg per day.

13~~17~~. The pharmaceutical composition according to any one of claims 1 to 12~~16~~, wherein the compound is administered to the patient at a dose of 10 mg to 50 mg per day for 1 week to 5 weeks.

14~~18~~. A method of producing a pharmaceutical composition for treating or preventing a disease caused in the vagina or perivaginal area by a pathogenic virus, the composition comprising, as an active ingredient, a compound selected from the group consisting of an aniline derivative represented by the following general formula (I)



(I)

wherein W represents S or O,
pharmaceutically acceptable salts thereof, and hydrates thereof,

the method comprising the following steps of:

(a) mixing core particle raw materials contaning

needle-like and/or approximately column-like-shaped crystalline cellulose and a pharmaceutically acceptable approximately spherical shaped additive to obtain a core particle mixture;

wherein the pharmaceutically acceptable approximately spherical shaped additive is lactose hydrate and/or corn starch,

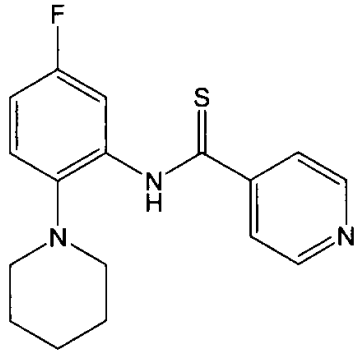
(b) dissolving or suspending the compound in a mixture of polysorbate 80 ~~a nonionic surfactant~~ and a solvent to obtain a mixed solution;

(c) contacting the core particle mixture obtained in the step (a) with the mixed solution obtained in the step (b) to obtain core particles containing the compound, the needle-like and/or approximately column-like-shaped crystalline cellulose, the approximately spherical shaped additive and the nonionic surfactant;

(d) coating the core particles obtained in the step (c) and drying, to obtain a granular preparation comprising the core particles and a coating layer coating the particles in which voids are formed between the crystalline cellulose and the approximately spherical shaped additive, and

(e) processing the resulting granular preparation to obtain a vaginal insert in the form of a vaginal tablet, a vaginal suppository or a vaginal capsule.

15~~19~~. The production method according to claim 14~~18~~, wherein the compound is a compound selected from the group consisting of an aniline derivative represented by the following formula (I-a):



(I-a)

, pharmaceutically acceptable salts thereof, and hydrates thereof.

16~~20~~. The production method according to claim 14~~18~~ or 15~~19~~, wherein at least part of the compound and at least part of the nonionic surfactant are retained in voids formed in the core particles.

17~~21~~. The production method according to any one of claims 14~~18~~ to 16~~20~~, wherein the step (e) is a step of tableting the granular preparation to obtain a vaginal tablet.

18~~22~~. The production method according to any one of claims 14~~18~~ to 17~~21~~, wherein in the step (b), the nonionic surfactant is mixed in an amount of 2 times or less compared to the compound.

19~~23~~. The production method according to any one of claims 14~~18~~ to 17~~21~~, wherein in the step (b), the nonionic surfactant is mixed in an amount of 1.5 times or less compared to the compound.

20~~24~~. The production method according to any one of claims 14~~18~~ to 19~~23~~, wherein the nonionic surfactant is contained in an amount of 1.5% by weight or more and less than 10% by weight with respect to the total amount of the pharmaceutical composition.

~~25. The production method according to any one of claims 18 to 23, wherein the nonionic surfactant is contained in an amount of 7 to 8% by weight with respect to the total amount of the pharmaceutical composition.~~

~~26. The production method according to any one of claims 18 to 25, wherein the nonionic surfactant is polysorbate.~~

21~~27~~. The production method according to any one of claims 14~~18~~ to 20~~26~~, wherein the pathogenic virus is human papillomavirus or herpes simplex virus.

22~~28~~. The production method according to any one of claims 14~~18~~ to 20~~26~~, wherein the disease is cervical cancer or cervical intraepithelial neoplasia.

~~29. The production method according to any one of claims 18 to 26, wherein the disease is condyloma acuminata.~~