Claims

1. Crystalline form of agomelatine, its X-ray diffraction diagram having the following values for Bragg angle 2θ:

2θ°
10.557
13.301
16.145
17.286
17.841
19.359
20.089
23.366
24.944
26.128

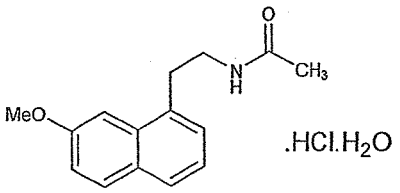
including crystals whose peak diffraction angles are within 2θ±0.2° of the above.

2. Crystalline form of agomelatine, its X-ray diffraction diagram having the following values for interplanar crystal spacing d, Bragg angle 2θ and relative intensity:

2θ°	d(Å)	Relative intensity (I%)
10.557	8.3725	32.35
13.301	6.6509	11.45
16.145	5.4855	10.60
17.286	5.1258	6.19
17.841	4.9675	100.00
19.359	4.5813	10.83
20.089	4.4164	11.77
23.366	3.8040	29.82
24.944	3.5667	21.60
26.128	3.4078	12.47

including crystals whose peak diffraction angles are within 2θ±0.2° of the above.

3. The preparation method for the crystalline form of agomelatine according to claim 1 or claim 2, wherein agomelatine compounds of formula (II) or (III) are dissolved in acetic acid, to which acetate is then added, followed by the addition of water dropwise to this reaction mixture, which is then agitated at a temperature of 17-23°C in order to bring about crystallization, with the crystals then being separated from the solution.



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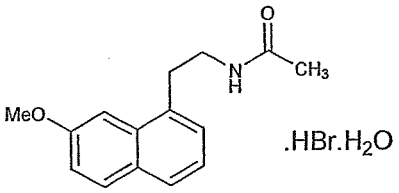

(III)

4. The preparation method according to claim 3, wherein the molar ratio of agomelatine compounds of formula (II) or (III) and acetate is in the order 1:1-1.5, most optimally 1:1-1.1.

5. The preparation method according to claim 3 or 4, wherein the ratio of volume of acetic acid to water is 1:10-30.

6. The preparation method according to any of claims 3-5, wherein the said acetate is potassium acetate or ammonium acetate.

7. The preparation method according to any of claims 3-6, wherein when the temperature of the resulting reaction mixture reaches 19-25°C, and especially when around 22°C or 23°C, water is added dropwise in order to bring about crystallization.

8. The preparation method according to any of claims 3-7, wherein water is added dropwise to the resulting reaction mixture which is then agitated at a temperature of 20°C in order to bring about crystallization.

9. The preparation method according to any of claims 3-8, wherein following the addition of the acetate, the reaction mixture is heated to 30-50°C, resulting in a clear solution; the said solution is then left to cool on its own, and water is added dropwise in order to bring about crystallization.

10. A pharmaceutical composition, including the crystalline form of agomelatine according to claim 1 or 2 and pharmaceutically acceptable adjuvants or excipients.

11. The pharmaceutical composition according to claim 10, used in the preparation of a medicament, with this medicament being used to treat diseases of the melatoninergic system.

12. The pharmaceutical composition according to claim 10, used in the preparation of a medicament, with this medicament being used to treat sleep disorders, stress, anxiety, seasonal affective disorder, severe depression,

cardiovascular diseases, digestive system diseases, insomnia and fatigue brought on by jet lag, schizophrenia, phobias, or depression.

13. The pharmaceutical application of the crystalline form of agomelatine according to claim 1 or 2, wherein the said pharmaceutical application relates to the treatment of diseases of the melatoninergic system.

14. The pharmaceutical application of the crystalline form of agomelatine according to claim 1 or 2, wherein the said pharmaceutical application relates to the treatment of sleep disorders, stress, anxiety, seasonal affective disorder, severe depression, cardiovascular diseases, digestive system diseases, insomnia and fatigue brought on by jet lag, schizophrenia, phobias, or depression.

The claims defining the invention are as follows:

1. Crystalline form of agomelatine, its X-ray diffraction diagram having the following values for Bragg angle 2θ:

2θ°
10.557
13.301
16.145
17.286
17.841
19.359
20.089
23.366
24.944
26.128

including crystals whose peak diffraction angles are within 2θ±0.2° of the above.

2. Crystalline form of agomelatine, its X-ray diffraction diagram having the following values for interplanar crystal spacing d, Bragg angle 2θ and relative intensity:

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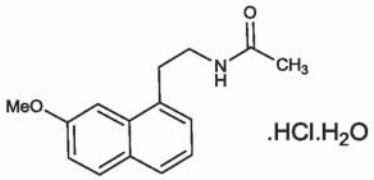
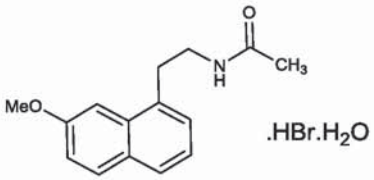
23.366	3.8040	29.82
24.944	3.5667	21.60
26.128	3.4078	12.47

including crystals whose peak diffraction angles are within 2θ±0.2° of the above.

3. A method for the preparation of the crystalline form of agomelatine according to claim 1 or claim 2, wherein agomelatine compounds of formula (II) or (III) are dissolved in acetic acid, to which acetate salt is then added, followed by the addition of water dropwise to this reaction mixture, which is then agitated at a temperature of 17-23°C in order to bring about crystallization, with the crystals then being separated from the solution.



(II)



(III)

4. The preparation method according to claim 3, wherein the molar ratio of agomelatine compounds of formula (II) or (III) and acetate salt is in the order 1:1-1.5.

5. The preparation method according to claim 4, wherein the molar ratio of agomelatine compounds of formula (II) or (III) and acetate salt is in the order , 1:1-1.1.

6. The preparation method according to any one of claims 3 to 5, wherein the ratio of volume of acetic acid to water is 1:10-30.

7. The preparation method according to any one of claims 3 to 6, wherein the said acetate salt is potassium acetate or ammonium acetate.

8. The preparation method according to any one of claims 3 to 6, wherein when the temperature of the resulting reaction mixture reaches 19-25°Cwater is added dropwise in order to bring about crystallization.

9. The preparation method according to claim 8, wherein the temperature of the resulting reaction mixture is around 22°C or 23°C.

10. The preparation method according to any one of claims 3 to 9, wherein water is added dropwise to the resulting reaction mixture which is then agitated at a temperature of 20°C in order to bring about crystallization.

11. The preparation method according to any one of claims 3 to 10, wherein following the addition of the acetate salt, the reaction mixture is heated to 30-50°C, resulting in a clear solution; the said solution is then left to cool on its own, and water is added dropwise in order to bring about crystallization.

12. A pharmaceutical composition, comprising the crystalline form of agomelatine according to claim 1 or 2 and a pharmaceutically acceptable adjuvant or excipient.

13. Use of the crystalline form of agomelatine according to claim 1 or 2, or the pharmaceutical composition according to claim 12, in the preparation of a medicament for the treatment of diseases of the melatoninergic system.

14. The use according to claim 13, for the treatment of sleep disorders, stress, anxiety, seasonal affective disorder, severe depression, cardiovascular diseases, digestive system diseases, insomnia and fatigue brought on by jet lag, schizophrenia, phobias, or depression.

15. A method for the treatment of diseases of the melatoninergic system in a patient, the method comprising administering to the patient an effective amount of the crystalline form of agomelatine according to claim 1 or 2, or the pharmaceutical composition according to claim 12.

16. The method according to claim 15, for the treatment of sleep disorders, stress, anxiety, seasonal affective disorder, severe depression, cardiovascular diseases, digestive system diseases, insomnia and fatigue brought on by jet lag, schizophrenia, phobias, or depression.