Claims

1. A process for the manufacture of crystalline vortioxetine HBr α-form, wherein said vortioxetine HBr α-form is characterized by XRPD reflections at 5.85, 9.30, 17.49 and 18.58 (°2θ) (±0.1°), the process comprising the steps of

a) obtaining a solution of vortioxetine in essentially pure toluene, wherein said essentially pure toluene contains more than 95 (w/v)% toluene;

b) mixing said solution obtained in step a) with HBr and C_1-C_3 carboxylic acid to obtain mixture b) at a temperature above 10 °C; and

c) collecting the precipitate obtained in step b).

2. The process according to claim 1 wherein the concentration of vortioxetine obtained in step a) is between 10 g/l toluene and 500 g/l toluene.

3. The process according to any of claims 1-2, wherein the concentration of vortioxetine obtained in step a) is between 40 g/l toluene and 200 g/l toluene.

4. The process according to any of claims 1-3, wherein the temperature of the solution obtained in step a) is between 0 °C and reflux.

5. The process according to any of claims 1-4, wherein the temperature of the solution obtained in step a) is between 25 °C and 40 °C.

6. The process according to any of claims 1-5, wherein the amount of HBr in step b) is between 0.9 and 2 mole equivalent relative to the amount of vortioxetine present in the solution obtained in step a).

7. The process according to any of claims 1-6 wherein the amount of HBr in step b) is between 1 and 1.3 mole equivalent relative to the amount of vortioxetine present in the solution obtained in step a).

8. The process according to any of claims 1-7, wherein the molar ratio HBr:C_1-C_3 carboxylic acid in step b) is 1:1 – to 1:10.

9: The process according to any of claims 1-8, wherein the molar ratio HBr: C_1-C_3 carboxylic acid in said mixture of HBr in acetic acid in step b) is 1:2 – to 1:4.

10. The process according to any of claims 1-9, wherein the temperature of mixture b) is above 10 °C and 40 °C or below.

11. The process according to any of claims 1-10, wherein said C_1-C_3 carboxylic acid is acetic acid.

12. The process according to any of claims 1-10, wherein said C_1-C_3 carboxylic acid is propionic acid.

13. The process according to any of claims 1-11 wherein said HBr and said C_1-C_3 carbolylic acid together is 33 (w/w)% HBr dissolved in acetic acid.