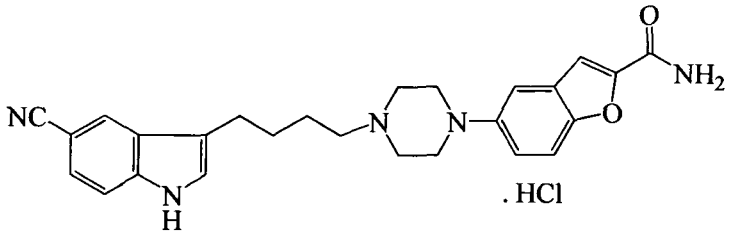
Abstract

The present invention provides a process for the preparation of form-XVI of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1 represented by the following structural formula.



Formula-1

We Claim:

1. A process for the preparation of form-XVI of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1, comprising of the following steps:

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide in a suitable acid,

b) adding suitable hydrochloric acid source to the reaction mixture,

c) filtering the reaction mixture,

d) adding suitable solvent to the filtrate obtained in step-(c),

e) stirring the reaction mixture,

f) filtering the precipitated solid and drying to provide form-XVI of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

2. A process according to claim-1,

in step-a) the suitable acid is selected from formic acid, acetic acid, propionic acid, butanoic acid, pentanoic acid, hexanoic acid and the like.

in step-b) the suitable hydrochloric acid source is selected from HCl gas, aqueous HCl, dry HCl, ethyl acetate-HCl, IPA-HCl, ethanol-HCl, methanol-HCl;

in step-d) the suitable solvent is selected from ester solvents, ketone solvents, chloro solvents, alcohol solvents, ether solvents, hydrocarbon solvents, polar aprotic solvents, polar solvents like water and mixture thereof; preferably the suitable solvent is selected from polar solvents such as water.

3. A process for the preparation of form-XVI of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1, comprising of the following steps;

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide in formic acid,

b) adding hydrochloric acid to the reaction mixture,

c) filtering the reaction mixture,

d) adding water to the filtrate obtained in step-(c),

e) stirring the reaction mixture,

f) filtering the precipitated solid and drying to provide form-XVI of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

4. 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride form-XVI obtained according to any of the preceding claims is characterized by its X-ray powder diffractogram having peaks at 7.8, 8.6, 10.5, 12.3, 14.8, 16.6, 19.4, 20.1, 21.1, 22.4, 23.6, 24.3, 24.5, 26.7, 27.2 and 31.6 ± 0.2 degrees of two-theta and P-XRD pattern as illustrated in figure-1.

5. 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride form-XVI obtained according to any of the preceding claims is further characterized by its DSC thermogram showing endotherms as illustrated in figure-2.

6. 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride form-XVI obtained according to any of the preceding claims having water content about 6.0 weight % to 8.0 weight %.

7. 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride Form-XVI obtained according to any of the preceding claims having purity by HPLC greater than 99.95 %.

8. A MCC pre-mixed vilazodone hydrochloride.

9. A MCC pre-mixed vilazodone hydrochloride having P-XRD pattern as illustrated in figure-4.

10. Use of MCC pre-mixed vilazodone hydrochloride in the preparation of pharmaceutical composition.

Dated this day 27th of December 2013.

Authorized Signatory

(Srinivasan Thirumalai Rajan)

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MSN Laboratories Private Limited

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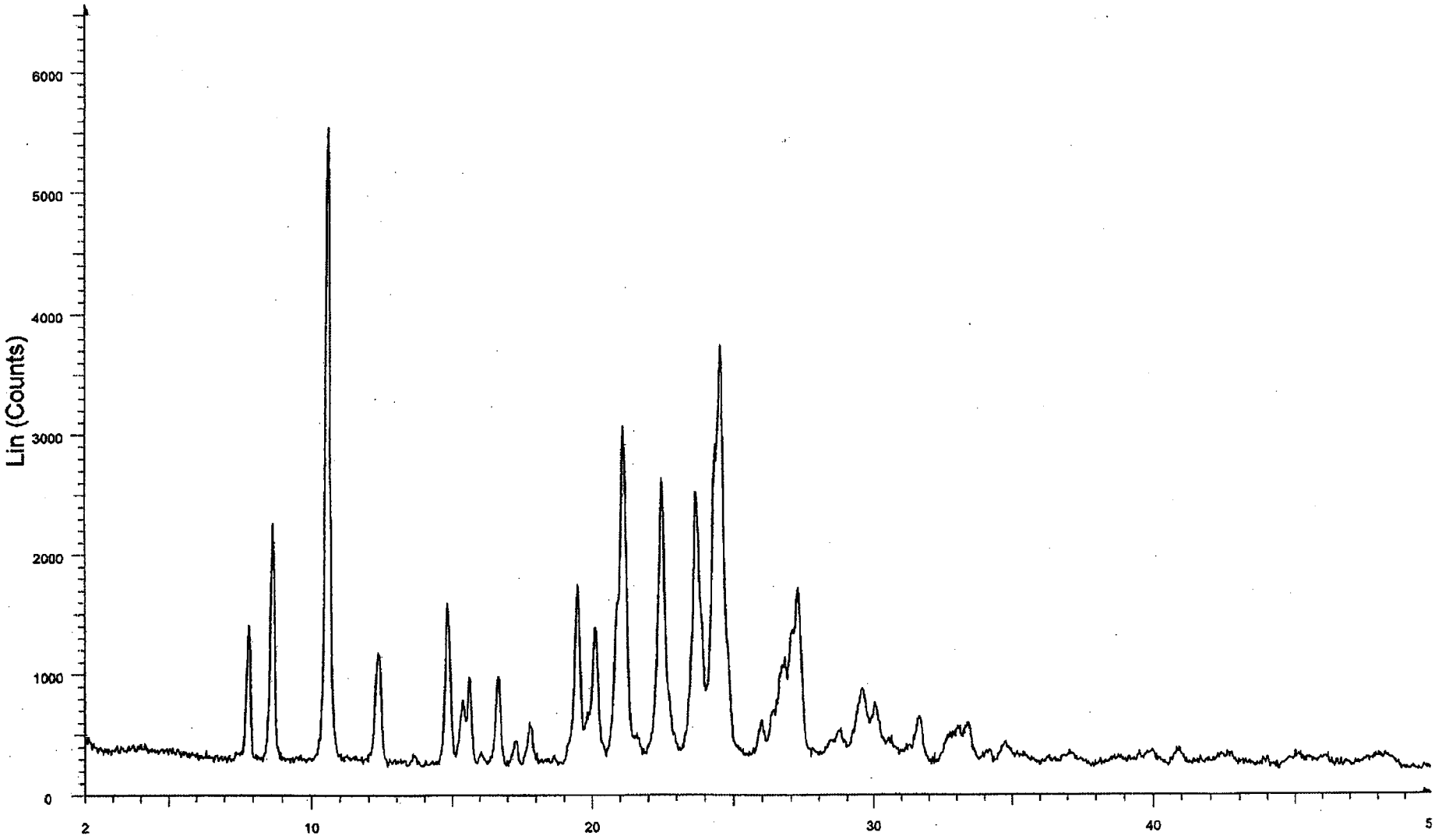

Figure-1

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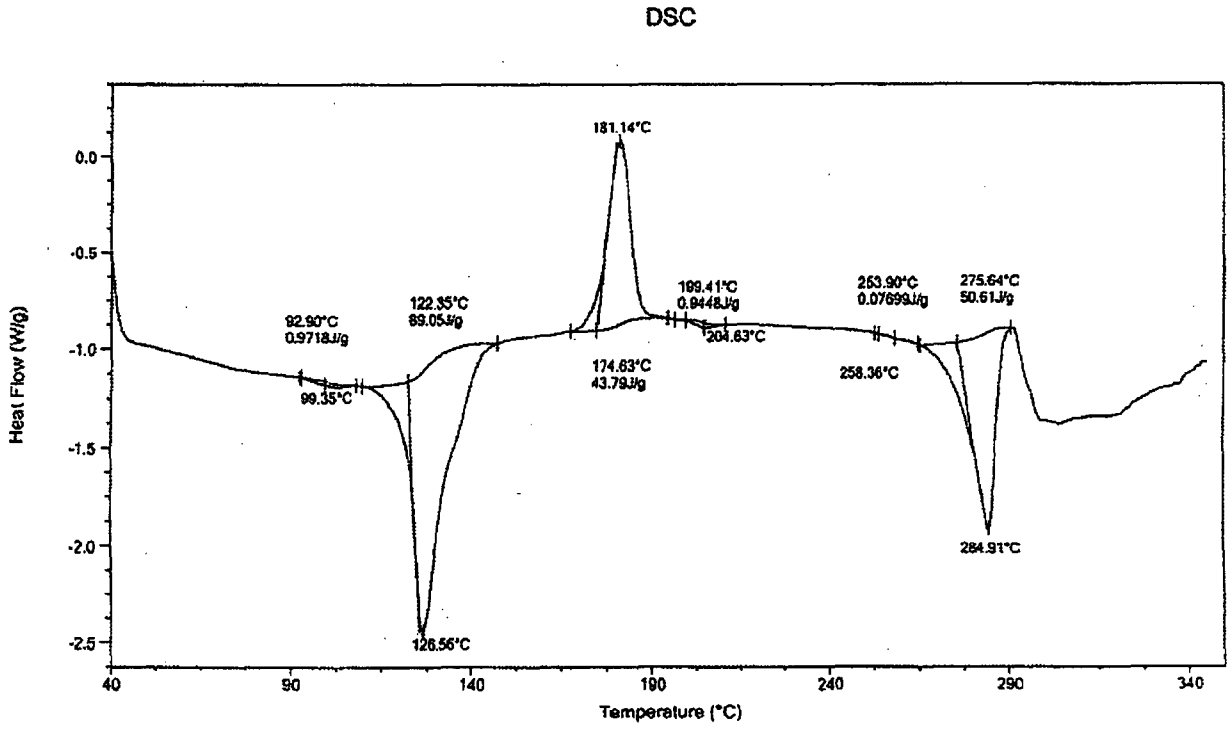

Figure-2

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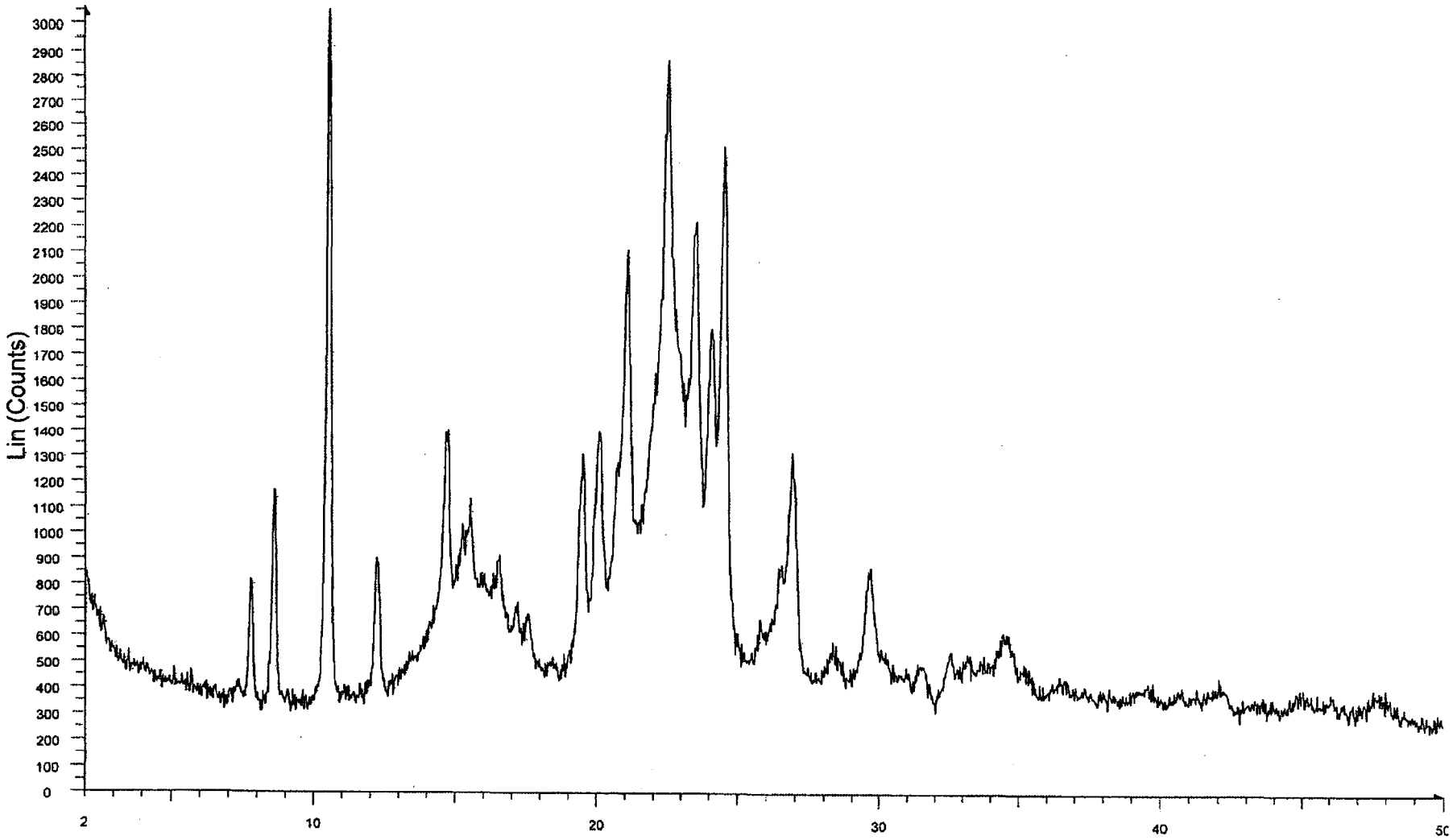

Figure-3

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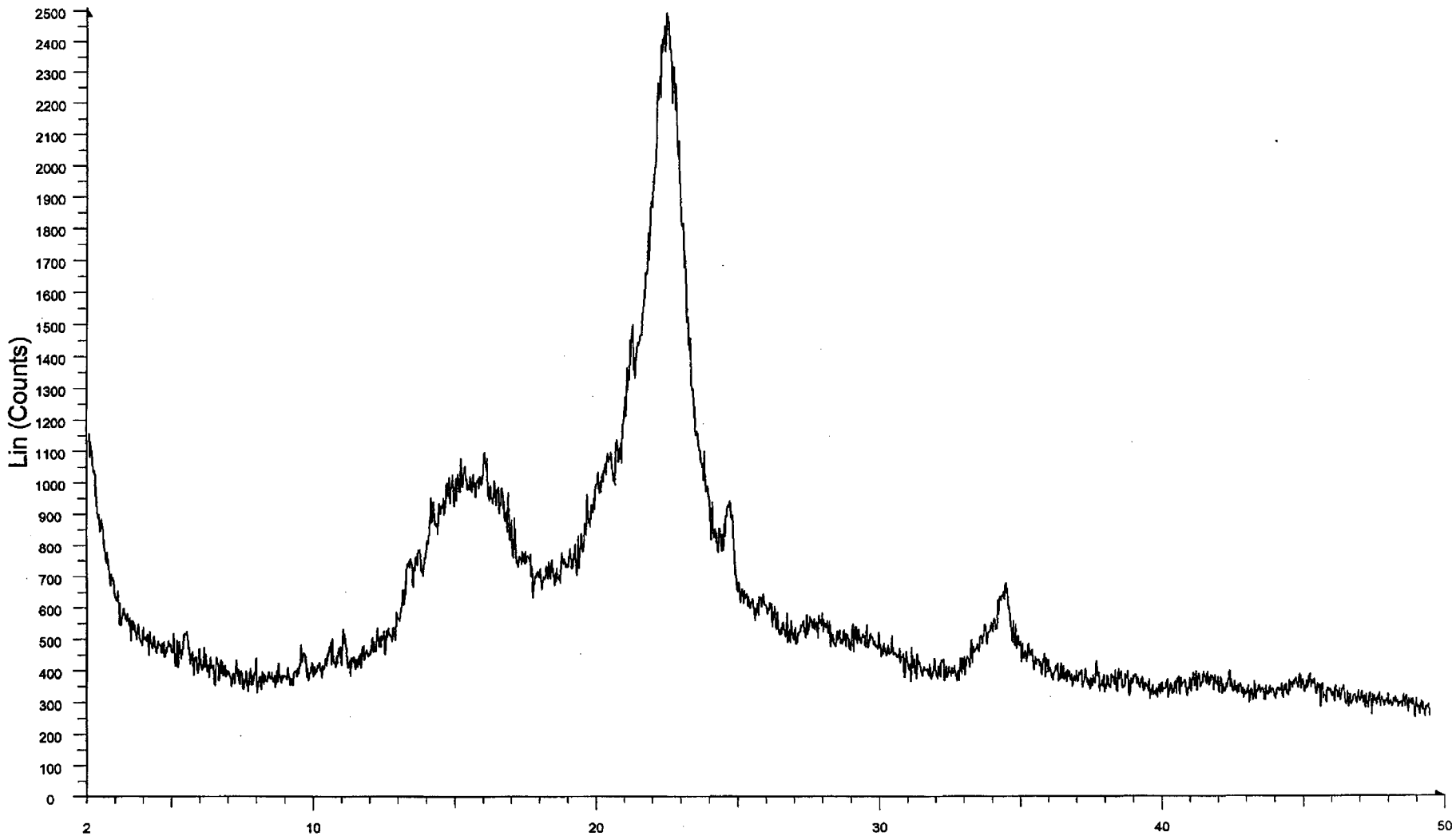

Figure-4

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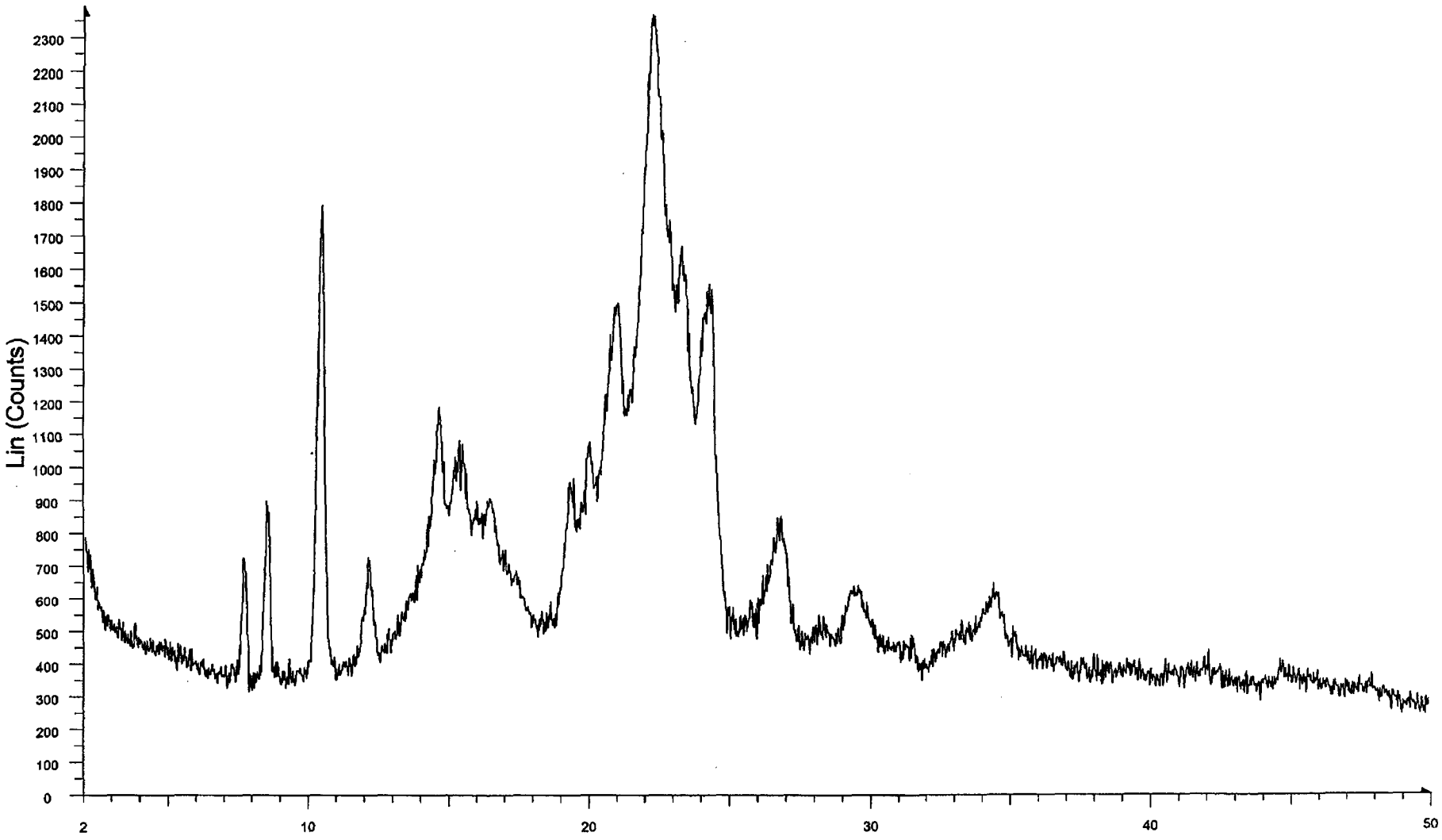

Figure-5

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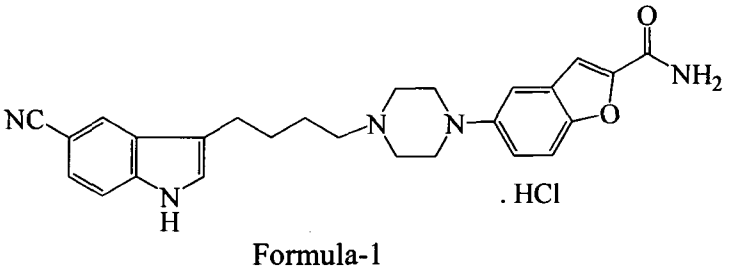
Field of the invention:

The present invention provides a process for the preparation of form-XVI of antidepressant drug i.e., 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1 represented by the following structural formula.



Formula-1

Back ground of the Invention:

US 5,532,241 (hereafter referred to as "241") first disclosed 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide and its hydrochloride salt compound of formula-1 which is commonly known as Vilazodone hydrochloride, an antidepressant agent, which acts as a serotonin reuptake inhibitor.

"241" first disclosed the process for the preparation of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide and its hydrochloride salt compound of formula-1 by reacting 5-(4-(4-(5-cyano-1H-indol-3-yl)butyl)piperazin-1-yl)benzofuran-2-carboxylic acid with 2-chloro-1-methylpyridinium methanesulfonate in the presence of N-methyl pyrrolidine and ammonia gas to provide vilazodone as free base. Further, vilazodone free base is dissolved in propanolic hydrochloric acid solution to precipitate hydrochloride salt of compound of formula-1.

US7834020 (hereafter referred to as "020") describes several crystalline forms of vilazodone hydrochloride, such as Form-I, II, III, IV, V, VI, VII, VIII, IX, X, XI, XIII, XIV, XV and XVI and process for their preparation.

"020" discloses the process for the preparation of vilazodone hydrochloride form-XVI (hereafter referred to as "form-XVI") using freeze-drying and spray drying methods. The process

for the preparation of vilazodone hydrochloride form-XVI by the said patent is critical, laborious, time consuming and not suitable for the commercial scale.

Hence in view of above, there is a need to find an efficient and industrially advantageous process which is commercial viable and which overcomes the problems associated with the prior art.

Brief description of the Invention:

The first aspect of the present invention is to provide a process for the preparation of form-XVI of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofurancarboxamide hydrochloride compound of formula-1, comprising of the following steps:

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide in a suitable acid,
b) adding a suitable hydrochloric acid source to the reaction mixture,
c) filtering the reaction mixture,
d) adding a suitable solvent to the filtrate obtained in step-(c),
e) stirring the reaction mixture,
f) filtering the precipitated solid and drying to provide form-XVI of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

The second aspect of the present invention is to provide a process for the preparation of micro crystalline cellulose (MCC) per-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1, which comprising of the following steps:

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide in a suitable acid,
b) adding a suitable hydrochloric acid source to the reaction mixture,
c) filtering the reaction mixture,
d) adding a suitable cellulose derivative to the filtrate obtained in step-(c),
e) adding a suitable solvent to the reaction mixture,
f) stirring the reaction mixture,

g) filtering the precipitated solid and drying to provide MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

The third aspect of the present invention is to provide a pre-mixed 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1 with an excipient.

The fourth aspect of the present invention is to provide a process for the preparation of MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1 with an excipient, which comprising of the following steps:

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide in a suitable acid,
b) adding a suitable hydrochloric acid source to the reaction mixture,
c) filtering the reaction mixture,
d) adding a suitable cellulose derivative to the filtrate obtained in step-(c),
e) distilling off the acid completely from the reaction mixture,
f) adding a suitable solvent to the compound obtained in step-(e),
g) stirring the reaction mixture,
h) filtering the precipitated solid and drying to provide MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

The fifth aspect of the present invention is to provide a process for the preparation of MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1 with an excipient, which comprising of the following steps:

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride in a suitable acid,
b) filtering the reaction mixture,
c) adding a suitable cellulose derivative to the filtrate obtained in step-(b),

d) distilling off the acid completely from the reaction mixture,
e) adding a suitable solvent to the compound obtained in step-(d),
f) stirring the reaction mixture,
g) filtering the precipitated solid and drying to provide MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

Brief description of the Drawings:

Figure 1: Illustrates the PXRD pattern of form-XVI of 5-[4-[4-(5-cyano-1H-indol-3- yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride obtained according to example-1.

Figure 2: Illustrates the DSC thermogram of form-XVI of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride obtained according to example-1.

Figure 3: Illustrates the PXRD pattern of MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride obtained according to example-2.

Figure 4: Illustrates the PXRD pattern of MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride obtained according to example-4.

Figure 5: Illustrates the PXRD pattern of MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride obtained according to example-5.

Detailed description of the Invention:

As used herein the term "suitable solvent" is selected from "alcoholic solvents" such as methanol, ethanol, isopropanol, n-propanol, n-butanol, iso-butanol, ethylene glycol and the like; "ester solvents" such as ethyl acetate, methyl acetate, n-butyl acetate, isobutyl acetate, sec-butyl acetate, isopropyl acetate and the like, "ether solvents" such as tetrahydrofuran, diethylether, methyl tert-butylether, 1,4-dioxane and the like; "hydrocarbon solvents" such as toluene, xylene, cyclohexane, hexane, heptane, n-pentane and the like; "chloro solvents" such as methylene chloride, ethylene dichloride, carbon tetrachloride, chloroform and the like; "polar aprotic

solvents" such as dimethyl formamide, dimethylacetamide, dimethylsulfoxide and the like; "nitrile solvents" such as acetonitrile, propionitrile, isobutyronitrile and the like; "ketone solvents" such as acetone, methyl isobutyl ketone, methyl ethyl ketone; polar solvent such as water and the like.

As used herein the term "suitable acid" is selected from formic acid, acetic acid, propionic acid, butanoic acid, pentanoic acid, hexanoic acid and the like.

The suitable hydrochloric acid source is selected from HCl gas, aqueous HCl, dry HCl, ethyl acetate-HCl, IPA-HCl, ethanol-HCl, methanol-HCl.

The term "MCC" used throughout the document is defined as micro crystalline cellulose.

The first aspect of the present invention provides a process for the preparation of form-XVI of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofurancarboxamide hydrochloride compound of formula-1, comprising of the following steps;

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide in a suitable acid,
b) adding a suitable hydrochloric acid source to the reaction mixture,
c) filtering the reaction mixture,
d) adding a suitable solvent to the filtrate obtained in step-(c),
e) stirring the reaction mixture,
f) filtering the precipitated solid and drying to provide form-XVI of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

Wherein,

in step-a) the suitable acid is selected from formic acid, acetic acid, propionic acid, butanoic acid, pentanoic acid, hexanoic acid and the like;

in step-b) the suitable hydrochloric acid source is selected from HCl gas, aqueous HCl, dry HCl, ethyl acetate-HCl, IPA-HCl, ethanol-HCl, methanol-HCl;

in step-d) the suitable solvent is selected from ester solvents, ketone solvents, chloro solvents, alcohol solvents, ether solvents, hydrocarbon solvents, polar aprotic solvents, polar solvents like water and mixture thereof; preferably the suitable solvent is selected from polar solvents such as water.

The preferred embodiment of the present invention provides a process for the preparation of form-XVI of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1, comprising of the following steps:

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide in formic acid,
b) adding hydrochloric acid to the reaction mixture,
c) filtering the reaction mixture,
d) adding water to the filtrate obtained in step-(c),
e) stirring the reaction mixture,
f) filtering the precipitated solid and drying to provide form-XVI of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

Further, 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride form-XVI obtained according to the above aspect of the present invention is characterized by its X-ray powder diffractogram having peaks at 7.8, 8.6, 10.5, 12.3, 14.8, 16.6, 19.4, 20.1, 21.1, 22.4, 23.6, 24.3, 24.5, 26.7, 27.2 and 31.6 ± 0.2 degrees of two-theta and P-XRD pattern as illustrated in figure-1.

The second aspect of the present invention provide a process for the preparation of micro crystalline cellulose (MCC) pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1, which comprising of the following steps:

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide in a suitable acid,
b) adding a suitable hydrochloric acid source to the reaction mixture,
c) filtering the reaction mixture,
d) adding a suitable cellulose derivative to the filtrate obtained in step-(c),
e) adding a suitable solvent to the reaction mixture,
f) stirring the reaction mixture,

g) filtering the precipitated solid and drying to provide MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

Wherein

in step-a) the suitable acid is same as defined in step-a) of the first aspect of the present invention;

in step-b) the suitable hydrochloric acid source is same as defined in step-b) of the first aspect of the present invention;

in step-d) the suitable cellulose derivatives is selected from cellulose acetate, cellulose nitrate, cellulose xanthate, carboxy methyl cellulose, micro crystalline cellulose, methyl cellulose, ethyl cellulose and hydroxy ethyl cellulose.

in step-e) the suitable solvent is same as defined in step-d) of the first aspect of the present invention.

The preferred embodiment of the present invention provides a process for the preparation of MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1, which comprising of the following steps:

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide in formic acid,
b) adding hydrochloric acid to the reaction mixture,
c) filtering the reaction mixture,
d) adding micro crystalline cellulose to the filtrate obtained in step-(c),
e) adding water to the reaction mixture,
f) stirring the reaction mixture,
g) filtering the precipitated solid and drying to provide MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofurancarboxamide hydrochloride compound of formula-1.

The process according to the present invention involves vilazodone hydrochloride form-XVI comprising of pharmaceutical excipient.

Further, the present invention also provides a pharmaceutical composition comprising the stable form-XVI of vilazodone hydrochloride together with one or more pharmaceutically acceptable carriers, excipients or diluents.

The third aspect of the present invention provides MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofurancarboxamide hydrochloride compound of formula-1.

The P-XRD of pre-mixed form of vilazodone hydrochloride obtained according to the present invention is shown in figure-4.

The fourth aspect of the present invention provides a process for the preparation of MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1 with an excipient, which comprising of the following steps:

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide in a suitable acid,
b) adding a suitable hydrochloric acid source to the reaction mixture,
c) filtering the reaction mixture,
d) adding a suitable cellulose derivative to the filtrate obtained in step-(c),
e) distilling off the acid completely from the reaction mixture,
f) adding a suitable solvent to the compound obtained in step-(e),
g) stirring the reaction mixture,
h) filtering the precipitated solid and drying to provide MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

Wherein,

in step-a) the suitable acid is selected from formic acid, acetic acid, propionic acid, butanoic acid, pentanoic acid, hexanoic acid and the like;

in step-b) the suitable hydrochloric acid source is selected from HCl gas, aqueous HCl, dry HCl, ethyl acetate-HCl, IPA-HCl, ethanol-HCl, methanol-HCl;

in step-d) the suitable cellulose derivatives is selected from cellulose acetate, cellulose nitrate,

cellulose xanthate, carboxy methyl cellulose, micro crystalline cellulose, methyl cellulose, ethyl cellulose and hydroxy ethyl cellulose;

in step-f) the suitable solvent is selected from ester solvents, ketone solvents, chloro solvents, alcohol solvents, ether solvents, hydrocarbon solvents, polar aprotic solvents, polar solvents like water and mixture thereof; preferably the suitable solvent is selected from ester solvents such as ethyl acetate.

The preferred embodiment of the present invention provides a process for the preparation of MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1, which comprising of the following steps:

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide in formic acid,
b) adding hydrochloric acid to the reaction mixture,
c) filtering the reaction mixture,
d) adding micro crystalline cellulose to the filtrate obtained in step-(c),
e) distilling off the formic acid completely from the reaction mixture,
f) adding ethyl acetate to the compound obtained in step-(e),
g) stirring the reaction mixture,
h) filtering the precipitated solid and drying to provide MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

The fifth aspect of the present invention provides a process for the preparation of per-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1 with an excipient, which comprising of the following steps;

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride in a suitable acid,
b) filtering the reaction mixture,
c) adding a suitable cellulose derivative to the filtrate obtained in step-(b),
d) distilling off the acid completely from the reaction mixture,
e) adding a suitable solvent to the compound obtained in step-(d),

f) stirring the reaction mixture,

g) filtering the precipitated solid and drying to provide MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

Wherein,

in step a) the suitable acid is same as defined in step-a) of the first aspect of the present invention;

in step-c) the suitable cellulose derivatives is same as defined in step-d) of the fourth aspect of the present invention;

in step-e) the suitable solvent is same as defined in step-f) of the fourth aspect of the present invention.

The preferred embodiment of the present invention provides a process for the preparation of MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1, which comprising of the following steps:

a) Dissolving the 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride in formic acid,

b) filtering the reaction mixture,

c) adding micro crystalline cellulose to the filtrate obtained in step-(b),

d) distilling off the formic acid completely from the reaction mixture,

e) adding ethyl acetate to the compound obtained in step-(d),

f) stirring the reaction mixture,

g) filtering the precipitated solid and drying to provide MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

PXRD analysis of compound produced by the present invention were carried out using BRUKER/AXS X-Ray diffractometer using Cu Kα radiation of wavelength 1.5406 A° and continuous scan speed of 0.03°/min.

Differential scanning calorimetric (DSC) analysis was performed with Q10 V9.6 Build 290 calorimeter. Samples of about 2 to 3 milligrams held in a closed pan were analyzed at a heating rate of 10° per minute.

HPLC Method of Analysis:

5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride compound of formula-1.

Apparatus: A liquid chromatographic system is to be equipped with variable wavelength UV-detector; Column: Symmetry C18, 150 x 4.6mm, 3.5 µm (or) equivalent; Flow rate: 1.0 ml/min; Wavelength: 242 nm; Column Temperature: 40°C; Injection volume: 5 µL; Run time: 35 min; Diluent: Water : Isopropyl alcohol (1:1) v/v; Needle wash: Water : Isopropyl alcohol (1:1) v/v; Elution: Gradient; Mobile phase-A: Buffer (100%); Mobile phase-B: Acetonitrile: Buffer (70:30) v/v; Buffer: 2.72 grams of potassium dihydrogen phosphate and 3.0 grams of 1-Octane sulphonic acid in 1000 ml of water. Adjust pH to 2.0 with diluted orthophosphoric acid and filtered through 0.22µm Nylon membrane filter paper and sonicate to degas it.

The compound produced by the present invention can be further micronized or milled to get the desired particle size to achieve desired solubility profile based on different forms of pharmaceutical composition requirements. Techniques that may be used for particle size reduction include, but not limited to ball, roller and hammer mills, and jet mills. Milling or micronization may be performed before drying, or after the completion of drying of the product.

The process described in the present invention was demonstrated in examples illustrated below. These examples are provided as illustration only and therefore should not be construed as limitation of the scope of the invention.

Examples:

Example-1: Preparation of Form-XVI of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride [Formula-1]

5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide (10 gms) was added to formic acid (25 ml) at 25-30°C and stirred for 15 minutes at the same temperature. Hydrochloric acid (2.3 ml) was slowly added to the reaction mixture at 25-30°C. Filter the reaction mixture and washed with formic acid (5.0 ml) at 25-30°C. Water (100 ml) was slowly added to the obtained filtrate at 25-30°C and stirred for 1 hour at the same temperature. Filtered the precipitated solid and washed with water. To the obtained wet solid, water (100 ml) was added at 25-30°C and stirred for 1 hour at the same temperature. Filtered the solid, washed with water and dried to get the title compound.

Yield: 8.1 gms.

The PXRD of the obtained compound is shown in figure-1.

Water content: 7.2 % w/w.

Formic acid content: 4417 ppm.

Purity by HPLC: 99.97 %.

Example-2: Preparation of MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride [Formula-1]

5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide (10 gms) was added to formic acid (25 ml) at 25-30°C and stirred for 15 minutes at the same temperature. Hydrochloric acid (2.3 ml) was slowly added to the reaction mixture at 25-30°C. Filter the reaction mixture and washed with formic acid (5.0 ml) at 25-30°C. Micro crystalline cellulose (10 gms), followed by water (100 ml) was slowly added to the obtained filtrate at 25-30°C and stirred for 1 hour at the same temperature. Filtered the precipitated solid and washed with water. To the obtained wet solid, water (100 ml) was added at 25-30°C and stirred for 1

hour at the same temperature. Filtered the solid, washed with water and dried to get the title compound.

Yield: 8.0 gms.

The PXRD of the obtained compound is shown in figure-3.

Water content: 7.6 % w/w.

Formic acid content: 3465 ppm.

Purity by HPLC: 99.95 %.

Example-3: Preparation of MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride [Formula-1]

5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide (10 gms) was added to formic acid (30 ml) at 25-30°C and stirred for 15 minutes at the same temperature. Hydrochloric acid (2.5 ml) was slowly added to the reaction mixture at 25-30°C. Filter the reaction mixture and washed with formic acid (10 ml) at 25-30°C. Micro crystalline cellulose (20.0 gms) was added to the reaction mixture at 25-30°C. Distilled off the formic acid completely from the reaction mixture under vacuum below 85°C. Ethyl acetate (300 ml) was added to the obtained compound at 15-20°C and stirred for 30 minutes at the same temperature. Filtered the solid, washed with ethyl acetate and dried to get the title compound.

Yield: 28.9.0 gms.

The PXRD of the obtained compound is shown in figure-4.

Example-4: Preparation of MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride [Formula-1]

5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride (10 gms) was added to formic acid (30 ml) at 25-30°C and stirred for 15 minutes at the same temperature. Filter the reaction mixture and washed with formic acid (10 ml) at 25-30°C. Micro crystalline cellulose (20.0 gms) was added to the reaction mixture at 25-30°C. Distilled off the formic acid completely from the reaction mixture under vacuum below 85°C. Ethyl acetate (300 ml) was added to the obtained compound at 15-20°C and stirred for 30 minutes at the same temperature. Filtered the solid, washed with ethyl acetate and dried to get the title compound.

Yield: 29.2. gms.

The PXRD of the obtained compound is shown in figure-4.

Example-5: Preparation of MCC pre-mixed form of 5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride [Formula-1]

5-[4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-2-benzofuran carboxamide hydrochloride (10 gms) was added to formic acid (30 ml) at 25-30°C and stirred for 15 minutes at the same temperature. Filter the reaction mixture and washed with formic acid (10 ml) at 25-30°C. Micro crystalline cellulose (20.0 gms) was added to the reaction mixture at 25-30°C. Distilled off the formic acid completely from the reaction mixture under vacuum below 85°C. Water (300 ml) was added to the obtained compound at 15-20°C and stirred for 30 minutes at the same temperature. Filtered the solid, washed with water and dried to get the title compound. Yield: 29.2. gms.

The PXRD of the obtained compound is shown in figure-5.