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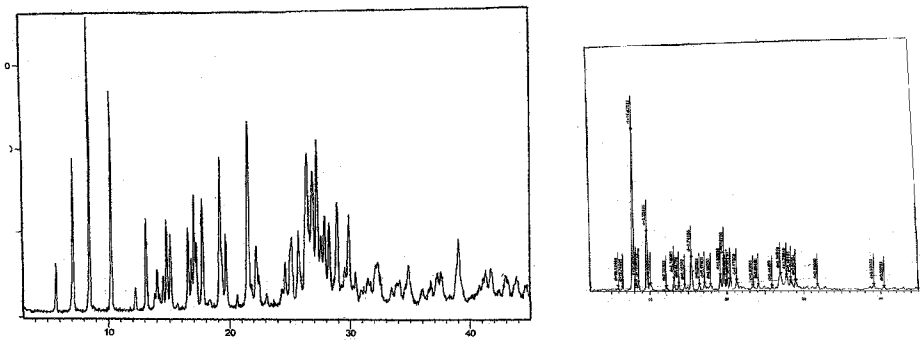
(54) **Title:** NOVEL CRYSTALLINE FORMS OF MOXIFLOXACIN HYDROCHLORIDE AND PROCESS FOR PREPARATION THEREOF



(57) **Abstract:** Novel crystalline forms of moxifloxacin hydrochloride and process for preparation thereof.

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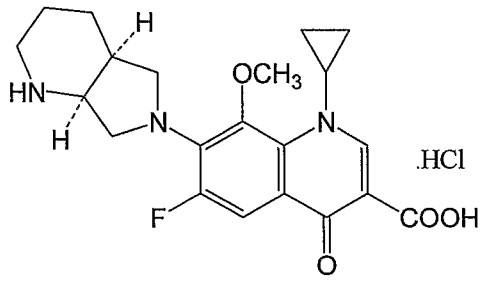
Novel crystalline forms of Moxifloxacin Hydrochloride and Process for Preparation thereof.

Field of the Invention:

The present invention relates to a novel crystalline forms of Moxifloxacin Hydrochloride, Particularly the present invention relates to a novel crystalline Form-X and Form-Y of Moxifloxacin Hydrochloride and process for preparing the same, Moxifloxacin hydrochloride chemically known as 1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridine-6-yl]-4-oxo-3-quinoline carboxylic acid hydrochloride compound of formula (I) as shown below.



Formula (I)

Moxifloxacin monohydrochloride is a synthetic broad-spectrum antibacterial agent. The active moiety, Moxifloxacin has been shown to be clinically active against most strains of microorganisms such as aerobic gram-positive microorganism including staphylococcus aureus, streptococcus pneumonia (penicillin-susceptible strains) and streptococcus pyogenes, aerobic gram-negative microorganisms including haemophilus influenza hemophilus parainfluenzae, klebisiella pneumonia.

BACKGROUND OF THE INVENTION

Polymorphism can be defined as the ability of the same chemical substance to exist in different crystalline structures. The different structures are referred to as polymorphs, polymorphic modification or polymorphic Forms.

Moxifloxacin hydrochloride is 1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7[(4aS, 7aS)-octahydro-6H-pyrrolo[3,4-b]pyridine-6-yl]-4-oxo-3-quinolinecarboxylic acid monohydrochloride, which is a hydrochloric acid salt of 1-Cyclopropyl-6-fluoro-1,4-

dihydro-8-methoxy-7[(4aS, 7aS)-octahydro-6H-pyrrolo[3,4-b]pyridine-6-yl]-4-oxo-3-quinolinecarboxylic acid in 1:1 mole ratio.

As a molecule Moxifloxacin hydrochloride is described U.S. 5,607,953, of which entire content is incorporated by reference herein. However, it is known that polymorphic forms of the same drug may have substantial differences in certain pharmaceutically important properties such as dissolution characteristics and bioavailability as well as stability of the drug. Further, more different crystalline form may have difference particle size, hardness and glass transition temperature. Thus, one crystalline form may provide significant advantages over other crystalline forms of the same drug in solid dosage form manufacture process such as accurate measurement of the active ingredients, easier filtration, or more improved stability during granulation or storage. Further more, a particular process suitable for crystalline form may also provide drug manufacturers several advantage such economically or environmentally suitable solvents or process or higher purity or yield of the desired product.

U.S.patent No 5,849,752 and WO 2004/091619 incorporated by reference, disclosed certain specific crystalline forms of anhydrous moxifloxacin monohydrochloride. For convenience, the anhydrous crystalline form disclosed in the '752 and '091619 patent designated as "Form 1 and Form III" and the hydrated "Form II" in the '752 patent.

The '752 patent discloses a process for the preparation of Moxifloxacin hydrochloride monohydrate, which comprises of anhydrous Moxifloxacin hydrochloride is dissolved in ethanol either with water or without water and distilled off and dried under humid condition to get Prisms and needles type of monohydrate material.

The same patent discloses that anhydrous form is the only crystal modification known in the prior art and discloses it XRD and other spectral characteristics.

US 4,990,517 disclosed the process for isolation of similar quinoline derivatives, by evaporating the solvent completely after the addition of hydrochloric acid to quinoline base and isolated the solid by adding and washing with ethanol and optionally with water. After that the obtained product is completely dried under vacuum at higher temperature. But actual process for the preparation of anhydrous Moxifloxacin hydrochloride polymorphic Form-1 has not been disclosed in any literature.

When we attempted to get the Form-1 of Moxifloxacin hydrochloride in lab by using the same process disclosed for the similar derivatives of quinolone in the '517 patent, we were getting the crystalline monohydrate form contaminated with little amorphous product, due to the instability of anhydrous form, which get converted to monohydrate form.

Form-III prepared as per the patent '091619 examples, lead to initially anhydrous form, but when we kept it open for 30 mts., in petri dish and as well as in stability by a normal packing condition, it picked up moisture and converted to hydrated form.

WO 2005/054240 discloses two novel crystalline forms, designated as Form A and Form B and process for preparing the same. which comprises of dissolving Moxifloxacin anhydrous or monohydrate form in a suitable solvent like ethanol and isopropanol and refluxing the same and cooling the reaction then isolating the product (Form A) and the resulting product reslurrying in alcohol at reflux to get Form B. These two forms are characterized by X-ray diffraction and water content.

WO 2004 / 091619 patent disclose X-ray diffraction pattern of the Anhydrous Form I, the disclosed 2θ values are 5.8, 8.6, 10.3, 11.6, 13.6, 14.5, 15.0, 15.8, 17.3, 17.5, 18.3, 18.9, 19.3, 19.6, 20.6, 21.5, 22.5, 22.8, 23.0, 23.8, 24, 24.7, 25.0, 26.3, 27.0, 27.4, 27.8, 28.2, 29.4, 29.7, 30.0, 30.3, 31.3, 31.8, 34.5, 35.3, 37.1.
And also disclose the X-ray diffraction pattern of Anhydrous Form-III and 2θ values are 5.6, 7.1, 8.4, 8.8, 10.0, 10.4, 11.4, 12.2, 13.1, 13.9, 14.4, 14.7, 16.6, 16.9, 17.2, 17.7, 18.5, 19.1, 19.219.8, 20.1, 20.3, 21.1,21.5, 22.1, 22.6, 22.9, 23.5, 24.0, 24.6, 24.9, 25.8, 26.2, 26.6, 26.9, 27.2, 28.729.1, 29.7, 30.1, 31.4, 32.1, 37.3, 39.9, 40.8, 41.5, 42.2, 43.1.

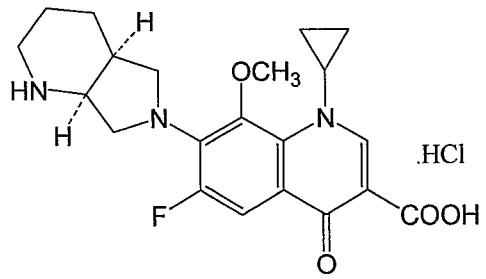
Hence, the object of the present invention is to provide the novel crystalline form of Moxifloxacin hydrochloride and process for preparing the same, which is stable as well as remains anhydrous for long term.

The crystalline form of the present invention is characterized by X-ray diffractogram pattern.

The novel crystalline form of Moxifloxacin hydrochloride may be well suited for pharmaceutical formulations and can be used in the antibacterial treatment.

BRIEF DESCRIPTION OF THE INVENTION

In accordance with the present invention, there is provided a novel crystalline anhydrous Form-X and Form-Y of Moxifloxacin hydrochloride and process for preparing the same, Moxifloxacin hydrochloride chemically known as 1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridine-6-yl]-4-oxo-3-quinoline carboxylic acid hydrochloride which have the following formula (I) as shown below.



Formula (I)

The first aspect of the present invention is to provide a novel crystalline anhydrous Form-X of Moxifloxacin hydrochloride, which is stable and can be scaled up with easier operation. The crystalline Form-X of moxifloxacin hydrochloride may be characterized by an X-ray diffraction pattern, expressed in terms of 2θ angles and obtained with a difractometer equipped with a copper K, X-radiation source, where in the X-ray powder diffraction pattern includes three or more peaks selected from the group consisting of peaks with 2 theta angles with 5.7, 7.1, 8.5, 10.2, 13.8, 14.0 15.1, 15.6,16.5, 16.8, 18.2, 19.7, 21.6, 22.2, 22.4, 24.3, 25.1, 25.7, 26.4, 28.9, 29.5, 29.8, 30.4, 32.0, 32.3, 33.3, 34.0, 34.7, 35.9, 36.6, 37.2, 37.5, 40.0, 41.2, 41.7, 42.9, 43.8, 44.7 degrees. The crystalline Form-X of Moxifloxacin hydrochloride may also be characterized by an X-ray diffraction pattern, expressed in terms of 2 theta angles and obtained with a difractometer equipped with a copper K, X-radiation source ,where in the X-ray powder diffraction pattern

includes difference of the 2 theta values between 10.2 and 12.2, no peaks were observed. The crystalline Form X of anhydrous Moxifloxacin hydrochloride in the composition of this aspect of the invention may be characterized by the XRD pattern as described.

The second aspect of the present invention is to provide the process for preparing the crystalline Form-X of Moxifloxacin hydrochloride compound of formula(I) which comprises;

i) Refluxing the Moxifloxacin hydrochloride azeotropically in a suitable hydrocarbon solvents,

ii) Isolating the product by cooling and filtration and drying the material to get the Moxifloxacin hydrochloride Form-X.

And to a pharmaceutical composition that includes the crystalline Form-X of Moxifloxacin hydrochloride and one or more pharmaceutically acceptable carriers are diluents. The pharmaceutical composition may also include one or more additional active ingredients.

The invention also relates to a method of preventing or treating allergic syndromes, by administering to a patient in need of such treatment an effective amount of crystalline Form-X of anhydrous Moxifloxacin monohydrochloride.

The Third aspect of the present invention is to provide a novel crystalline Form-Y of Moxifloxacin hydrochloride, which is also stable and can be scaled up with easier operation. The crystalline Form-Y of Moxifloxacin hydrochloride may be characterized by an X-ray defraction pattern, expressed in terms of 2θ angles and obtained with a difractometer equipped with a copper K X-radiation source, where in the X-ray powder diffraction pattern includes three or more peaks selected from the group consisting of peaks with 2 theta angles with 5.8, 6.4, 7.7, 8.1,8.4, 9.5, 10.0, 12.0, 13.0, 13.7, 14.5, 15.4, 16.4, 17.1, 17.9, 19.1, 19.6, 19.9, 20.4, 21.2, 23.3, 24.0, 25.8, 26.9, 27.7, 28.3, 28.9, 31.8, 39.1, 40.4 degrees.The crystalline Form-Y of Moxifloxacin hydrochloride may also be characterized by an X-ray diffraction pattern,expressed in terms of 2 theta angles and obtained with a difractometer equipped with a copper K, X-radiation source, where in the

X-ray powder diffraction pattern includes two or more peaks selected from the group consisting of with 2 theta angles 6.4, 7.7, 8.1, 16.4, 19.9, 23.3, 25.8, 27.7, and 40.4. The crystalline Form-Y of Moxifloxacin hydrochloride in the composition of this aspect of the invention may be characterized by the XRD pattern as described.

The fourth aspect of the present invention is to provide the process for preparing the crystalline Form-Y of Moxifloxacin hydrochloride which comprises of.

i) Heating the suspended Moxifloxacin in alcoholic solvents,

ii) Dissolving the compound by adjusting the pH,

iii) Filtering, and adjusting the pH,

iv) Stirring for 1 to 3 hours,

v) Isolating the product by filtration and drying the material to get the Moxifloxacin hydrochloride Form-Y.

And to a pharmaceutical composition that includes the crystalline Form-Y of Moxifloxacin hydrochloride and one or more pharmaceutically acceptable carriers are diluents. The pharmaceutical composition may also include one or more additional active ingredients.

The invention also relates to a method of preventing or treating allergic syndromes, by administering to a patient in need of such treatment an affective amount of crystalline Form-Y of Moxifloxacin hydrochloride.

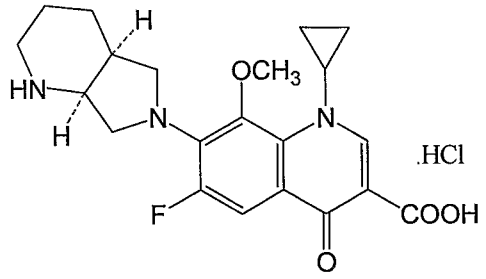
DESCRIPTION OF THE ACCOMPANYING DRAWINGS

Figure-1 is a sample of X-ray powder difractogram of the crystalline Form-X of Moxifloxacin Hydrochloride.

Figure-2 is a sample of X-ray powder difractogram of the crystalline Form-Y of Moxifloxacin Hydrochloride.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a novel crystalline forms of Moxifloxacin Hydrochloride, Particularly the present invention relates to novel crystalline Form-X and Form-Y of Moxifloxacin Hydrochloride and process for preparing the same, Moxifloxacin hydrochloride is chemically known as 1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridine-6-yl]-4-oxo-3-quinoline carboxylic acid hydrochloride compound of formula (I) as shown below.



Formula (I)

A compound is a chemical substance that includes molecules of the same chemical structure. Pharmaceutically acceptable means that which is useful in preparing a pharmaceutical composition that is generally non-toxic and is not biologically undesirable and includes that which is acceptable for veterinary use and human pharmaceutical use.

Accordingly the first aspect of the invention is to provide the new crystalline Form-X of anhydrous Moxifloxacin monohydrochloride, which is different from the Form- I and Form- III of the '752 and 091619 patents. A process including refluxing azeotropically a mixture of moxifloxacin hydrochloride and a solvent selected from the group consisting of aliphatic or aromatic hydrocarbons solvent to form a mixture, cooling the refluxed mixture until solid separates, and isolating said solid thereby obtaining said crystalline Form-X of Moxifloxacin hydrochloride.

The crystalline Form-X of moxifloxacin monohydrochloride produced by the inventors was characterized by an X-ray powder diffraction pattern. An example of one of X-ray

diffraction analysis is shown in Figure-1, and the characteristic 2-theta values (in degrees) in the X-ray diffractograms are as follows;
5.7, 7.1, 8.5, 10.2, 13.8, 14, 15.1, 15.6, 16.5, 16.8, 18.2, 19.7, 21.6, 22.2, 22.4, 24.3, 25.1, 25.77, 26.428.9, 29.5, 29.8, 30.4, 32 ,32.3, 33.3, 34, 34.7, 35.9, 36.6, 37.2, 37.5, 40, 41.2, 41.7, 42.9, 43.8, 44.7

The X-ray diffractogram was measured on a Siemens D/Max-5000 model powder X-ray diffractometer with Cu K alpha-1 radiation source.

Comparing the XRD data as disclosed in prior art above (WO 2004 / 091619) at certain peaks provide the best way of characterizing the crystalline Form-X of anhydrous moxifloxacin monohydrochloride and of differentiating it from the Forms I and III.Very few of such peaks are needed to allow for such characterization and differentiation, including presence of the crystalline Form-X of anhydrous Moxifloxacin monohydrochloride in mixtures with other forms of Moxifloxacin. Thus, the crystalline Form-X of anhydrous moxifloxacin hydrochloride may also be characterized by an X-ray powder diffraction pattern includes absence of peaks at 2 theta values between 10.2 and 12.2 is the major difference from the anhydrous Form I and Form-III.

The second aspect of the present invention is to provide a process for preparing the crystalline Form-X of Moxifloxacin hydrochloride compound of formula (I) which comprises;

i) Refluxing azeotropically the Moxifloxacin hydrochloride in hydrocarbon solvents such as, cyclohexane, n-Heptane and Toluene,
ii) Isolating the material by cooling the reaction mass followed by filtering the separated solid and optionally washing the material with alcoholic solvent,
iii) Drying the compound under vacuum between 80 to 90°C to afford a Form X of anhydrous moxifloxacin hydrochloride.

The third aspect of the present invention provides new crystalline Form-Y of Moxifloxacin monohydrochloride, which is different from the Form I, Form-II and Form III of the '752 and 091619 patents and the present Form-X. A process including, heating the mixture of moxifloxacin and a solvent selected from the group of alcoholic solvent and adjusting the pH to 7.5 –8.5 with alkali solution and filtering to get a clear solution. Adjusting the pH of the filtrate to below 2.0 with aqueous HCl. and isolating the separated solid there by obtaining crystalline Form-Y of moxifloxacin hydrochloride.

The crystalline Form-Y of Moxifloxacin monohydrochloride produced by the inventors was characterized by an X-ray powder diffraction pattern. An example of one of X-ray diffraction analysis is shown in Figure- 2, and the characteristic 2-theta values (in degrees) in the X-ray diffractograms are as follows;
5.8, 6.4, 7.7, 8.1, 8.4, 9.5, 10.0, 12.0, 13.0, 13.7, 14.5, 15.4, 16.4, 17.1, 17.9, 19.1, 19.6, 19.9, 20.4, 21.2, 23.3, 24.0, 25.8, 26.9, 27.7, 28.29, 28.9, 31.8, 39.1, 40.4,

The fourth aspect of the present invention is to provide the process for preparing the crystalline Form-Y of Moxifloxacin hydrochloride which comprises of;

i) Charging the Moxifloxacin and alcoholic solvents such as Methanol, ethanol,propanol and butanol , preferably methanol and water,
ii) Heating the reaction mixture to 50-60°C,
iii) Dissolving the material by adjusting the pH to 7.5-8.5 using with aqueous alkaline solution like sodium hydroxide, potassium hydroxide and potassium carbonate preferably sodium hydroxide,
iv) Filtering the reaction mass through hyflow bed to get clear solution,
v) Adjusting the pH to below 2, preferably to below 1 and most preferably to 0.5 with aqueous HCl at below 15°C,
vi) Maintaining the reaction mass 30-60 min at below 15°C ,
vii) Isolating the separated solid by conventional method ,
viii) Optionally repeating the operation from step (i) to step(vii) to get high pure material,

ix) Drying the product at 60- 70 ^{O}C for 4-6 hours.

The present invention also discloses a process for the preparation of Moxifloxacin hydrochloride monohydrate which comprises of;

i) Reacting 1-cylcopropyl-6,7-difluoro-8-methoxy-4-oxo-1,4-dihydro-3-quinoline carboxylic acid with boric acid and acetic anhydride in presence of zinc chloride in a suitable solvent like acetic anhydride to afford (1-cyclopropyl -6,7-difluoro-8-methoxy, 4-oxo-1,4-dihydro, quinoline-3-carboxylate-O^3, O^4)-bis—(acetate-O)boran, which in situ condensation with (S,S) 2,8, Diazabicylco (4,3,0) nonane in presence of base like triethylamine in a suitable solvent like acetonitrile and treating with aqueous hydrochloric acid gives 1-cylcopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-[(4aS, 7aS)-octahydro-6H-pyrrolo[3,4-b]lpyridin-6-yl)-4-oxo-3-quinoline carboxylic acid hydrochloride, which upon purifying with methanol and water as a solvent in presence of aqueous hydrochloric acid to give moxifloxacin hydrochloride monohydrate.

Another embodiment of the present invention discloses a process for the preparation of Anhydrous Moxifloxacin hydrochloride which comprises of;

i. Refluxing (azeotropically) Moxifloxacin hydrochloride monohydrate compound in a suitable solvent like toluene to get the anhydrous form of Moxifloxacin hydrochloride.

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.

Reference Example: Preparation of Moxifloxacin

A solution of 100g of 1-Cyclopropyl –6,7difluoro-1,4-dihydro-4-oxo-methoxyquinolone-3-carboxilic acid), 52gr of (S,S)2,8 diazabicyclo[4,3,0]nonane, 10gr of 1,8-diazabycyclo[5,4,0]undec-7-ene and 300ml of acetonitrile is heated to 65 –70°C temperature and stirred till the reaction get completed and evaporated the solvent. Added 5 %aqueous isopropylalcohol to the reaction mass and adjusted the pH to basic with caustic solution and then filtered the reaction mass. Combined the total filtrate and adjusted the pH to 5.0 to 6.0 with aqueous HCl.and isolated the separated solid at a temperature of 10-15°C to afford Moxifloxacin.

Example 1: Preparation of novel crystalline Form -Y of moxifloxacin hydrochloride.

Suspended 95grams of Moxifloxacin obtained as per the above mentioned process in a mixture of 600ml of Methanol and 66 ml of water. Heated the reaction mixture to 50-60°C.Dissolved the compound by adjusted the pH to 8.5 with aqueous sodium hydroxide solution then filtered through a hyflow bed. Adjusted the filtrate pH to 0.6 using aqueous hydrochloric acid at below 15°C and the Isolate the solid by filtration and dried the compound at 60-70°C for 4-6 hours to get the title compound crystalline Form-Y of Moxifloxacin hydrochloride.

Example 2: Preparation of novel crystalline Form -X of moxifloxacin hydrochloride.

50gr of Moxifloxacin hydrochloride Form-Y suspended in 400ml of n-Heptane. Azeotropically removed the water at reflux temperature. Cooled the reaction mixture to 25-35°C and stirred to get the solid. Isolated the solid by filtration and washed with isopropyl alcohol. Dried at 80-90°C under the vacuum to afford the novel crystalline Form-X of moxifloxacin Hydrochloride.
(Weight: 47.0grams, M.C by KF is 0.15%w/w).

Example 3: Preparation of novel crystalline form X of anhydrous moxifloxacin hydrochloride.

50gr of Moxifloxacin Hydrochloride Form-Y suspended in 400ml Toluene. Heated the reaction mixture to 110-112°C to reflux azeotropically. Isolating the product by cooled the reaction mixture to 25-35°C followed by filtration. Dried at 80-90°C under vacuum, to afford the novel crystalline Form-X of anhydrous Moxifloxacin hydrochloride.
(Weight: 45.0grams, M.C by KF method is 0.10%w/w, Purity by HPLC: 99.93%)

Example 4: Preparation of novel crystalline form X of anhydrous moxifloxacin hydrochloride.

50gr Moxifloxacin Hydrochloride was suspended in 400ml Toluene. Heated the reaction mixture to 110-112°C to reflux azeotropically. Isolating the production by cooled the reaction mixture to 25-35°C followed by filtration. Washed the material with isopropyl alcohol. Dried at 80-90°C under vacuum to afford the novel crystalline form X of anhydrous Moxifloxacin hydrochloride.
(Weight: 44.0grams, M.C by KF method is 0.18%w/w, Purity by HPLC: 99.94%)

Example 5: Preparation of novel crystalline form X of anhydrous Moxifloxacin hydrochloride

50g of 1-cyclopropyl –6,7-difluoro –1,4-difluoro-1, 4 – dihydro – 4 – oxo-8-methoxy quinolone-3-carboxilic acid , (S, S) diazabicyclo nonane and 5gr of 1,8-diazabicyclo [5,4,0] undec-7-ene (5g) in 300 ml acetonitrile heated to 65-75°C and stirred. Evaporated the solvent completely and added 5 % aqueous isopropyl alcohol. Adjusted the pH to 8.5 with caustic solution, then the reaction mass filtered. Adjusted the pH filtrate to 5 with aqueous hydrochloric acid. Cooled the reaction mixture to 10-15°C. Isolated the separated solid to afford moxifloxacin. This wet Moxifloxacin, suspended in 400 ml Toluene and heated 110-112°C to reflux azeotropically and then reaction mass is cooled to 25-35°C. Quenched the reaction mass with 200 ml of isopropyl alcohol and adjusted pH to .98 with hydrochloric acid in Isopropyl alcohol. Isolated the solid by filtration and washed the material with isopropyl alcohol. Dried at 80-90°C under vacuum to afford the novel crystalline form -X of anhydrous Moxifloxacin hydrochloride.
(Weight: 33.0 grams, M.C by KF method is 0.09%w/w, Purity by HPLC: 99.94%)

Example 6: One-pot Preparation of Moxifloxacin hydrochloride monohydrate.

Added 70gr of 1-Cyclopropyl-6,7-difluro-8-methoxy-4-oxo-1,4-dihyro-3-quinoline carboxylic acid to a solution of 14.7 gr of boric acid and175ml of acetic anhydride ,0.07g of zinc chloride at 25-45°C. Heated the reaction mixture to 100-120°C. Stirred for 90 min. Cooled the reaction mixture to 0-5°C. Isolated the material by filtration and washed with hexanes. A solution of 70g of the obtained wet material [(1-cylcopropyl)-6,7-difluoro-8-methoxy,-4-oxo-1,4-dihydro,quinoline -3-carboxylate-O^3, O^4)-bis-(acetate-O) boran], 30 g of [S, S]-2,8-diaza bicyclo (4,3,0)nonane, 30 ml of triethylamine and 300ml of acetonitrile is heated to reflux. Stirred at reflux for 90 mins. Distilled the solvent completely under reduced pressure at 85°C. Added 316ml of aqueous sodium hydroxide solution at 50-70°C. Heated the reaction mixture to 85-95°C and stirred for 2 hrs. Adjusted the pH of the reaction mixture to 9 with acetic acid at 25-35°C. Extracted the reaction mixture with methylene chloride and separated the organic phase. Distilled the

solvent completely under reduced pressure at 60°C. Dissolved the residue in 240ml of acetone at 40-50°C, stirred for 15 min. Adjusted the pH to 1.0 with hydrochloric acid at 40-50°C. Cooled to 10-15°C and stirred for 90min. Filtered the precipitated solid and washed with acetone to get 1-Cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridine-6-yl]-4-oxo-3-quinoline carboxylic acid hydrochloride which is further purified using 405ml of methanol and 45 ml of water. Dissolved the compound by adjusting the pH to 7.8 with aqueous sodium hydroxide solution at 50-60°C and treated with carbon. Filtered through hiflow and washed with methanol and water. Cooled the filtrate to 10-15°C. Adjusted the pH with hydrochloric acid and stirred for 90 min. Filtered the precipitated solid and washed with methanol. Dried the compound at 50-60°C until the water content reaches to 3-6%w/w to get Moxifloxacin hydrochloride monohydrate.

Yield : 50 gr

Example 7: Preparation of Anhydrous Moxifloxacin hydrochloride.

A suspension of 10 gr of Moxifloxacin hydrochloride monohydrate and toluene was heated to reflux in azeotropic mode till to get complete water traces. Cooled the mass to 25-35°C and filtered the solid, washed with isopropyl alcohol to get anhydrous Moxifloxacin hydrochloride.

Yield: 8 gr

We claim

1. A compound which is crystalline Form-X of anhydrous moxifloxacin hydrochloride.

2. The compound of claim 1 having an X-ray diffraction pattern, expressed in terms of 2 theta angles and obtained with a diffractometer equipped with a copper K X- Radiation source, where in said X-ray powder diffraction pattern includes peaks selected from the group consisting of peaks with the 2 theta angles of about 5.7, 7.1, 8.5, 10.2, 13.8, 14.0 15.1, 15.6, 16.5, 16.8, 18.2, 19.7, 21.6, 22.2, 22.4, 24.3, 25.1, 25.7, 26.4, 28.9, 29.5, 29.8, 30.4, 32.0, 32.3, 33.3, 34.0, 34.7, 35.9, 36.6, 37.2, 37.5, 40.0, 41.2, 41.7, 42.9, 43.8, 44.7 degrees.

3. A process for the preparation of a crystalline Form-X of moxifloxacin hydrochloride, said process comprising:
   a) refluxing azeotropically the moxifloxacin monohydrochloride Form-Y in a solvent selected from the group consisting of aliphatic or aromatic hydrocarbons,
   b) Cooling and isolated the solid separated material crystalline Form-X of anhydrous moxifloxacin hydrochloride,
   c) Optionally washing the above obtained product with alcoholic solvent comprising C_1-C_4 alcohols,
   d) Drying the product at 80 – 90°C under vacuum 750 Hg /mm.

4. The process for the preparation of a crystalline Form-X of Moxifloxacin Hydrochloride, said process comprising;
   a) Refluxing azeotropically the moxifloxacin in a solvent selected from the group consisting of aliphatic or aromatic hydrocarbons,
   b) Adjusting the pH 0.5 to 1.0 with HCl in alcoholic solvents C_1-C_4 at below 15°C,
   c) Filtering the isolated material and washing with alcoholic solvents comprising C_1-C_4 alcohol,
   d) Drying the product at 80 – 90 °C under vacuum 750 Hg /mm.

5. The process of claim 3(a) and 4(a), wherein said aliphatic or aromatic hydrocarbons solvents selected from group consisting of n-Hexane, n-Heptane, Cyclohexane, Toluene and Xylene.

6. A compound which is crystalline Form-Y of Moxifloxacin hydrochloride.

7. The compound of claim-6 having an X-ray diffraction pattern, expressed in terms of 2 theta angles and obtained with a diffractometer equipped with a copper K X- Radiation source, where in said X-ray powder diffraction pattern includes peaks selected from the group consisting of peaks with the 2 theta angles of about, 5.8, 6.4, 7.7, 8.1,8.4, 9.5, 10.0, 12.0, 13.0, 13.7, 14.5, 15.4, 16.4, 17.1, 17.9, 19.1, 19.6, 19.9, 20.4, 21.2, 23.3, 24.0, 25.8, 26.9, 27.7, 28.3, 28.9, 31.8, 39.1, 40.4 degrees.

8. A process for the preparation of a crystalline Form-Y of Moxifloxacin hydrochloride, said process comprising:
   a) Adding the moxifloxacin in a solvent selected from the group of alcoholic solvent comprising C_1-C_4 alcohol and water,
   b) Adjusting the pH of the reaction mass with alkaline solution to 7.5 - 8.5 at 50 to 60°C to get a clear solution ,
   c) Filtering the clear solution and adjusting the pH of the reaction mass to 0.5 to 1.0 at below 15°C with aqueous HCl,
   d) Filtering the isolated material and washing with alcoholic solvents comprising C_1-C_4 alcohol,
   e) Drying the material at 60-70°C for 4-6 hours gave crystalline Form-Y of Moxifloxacin hydrochloride.

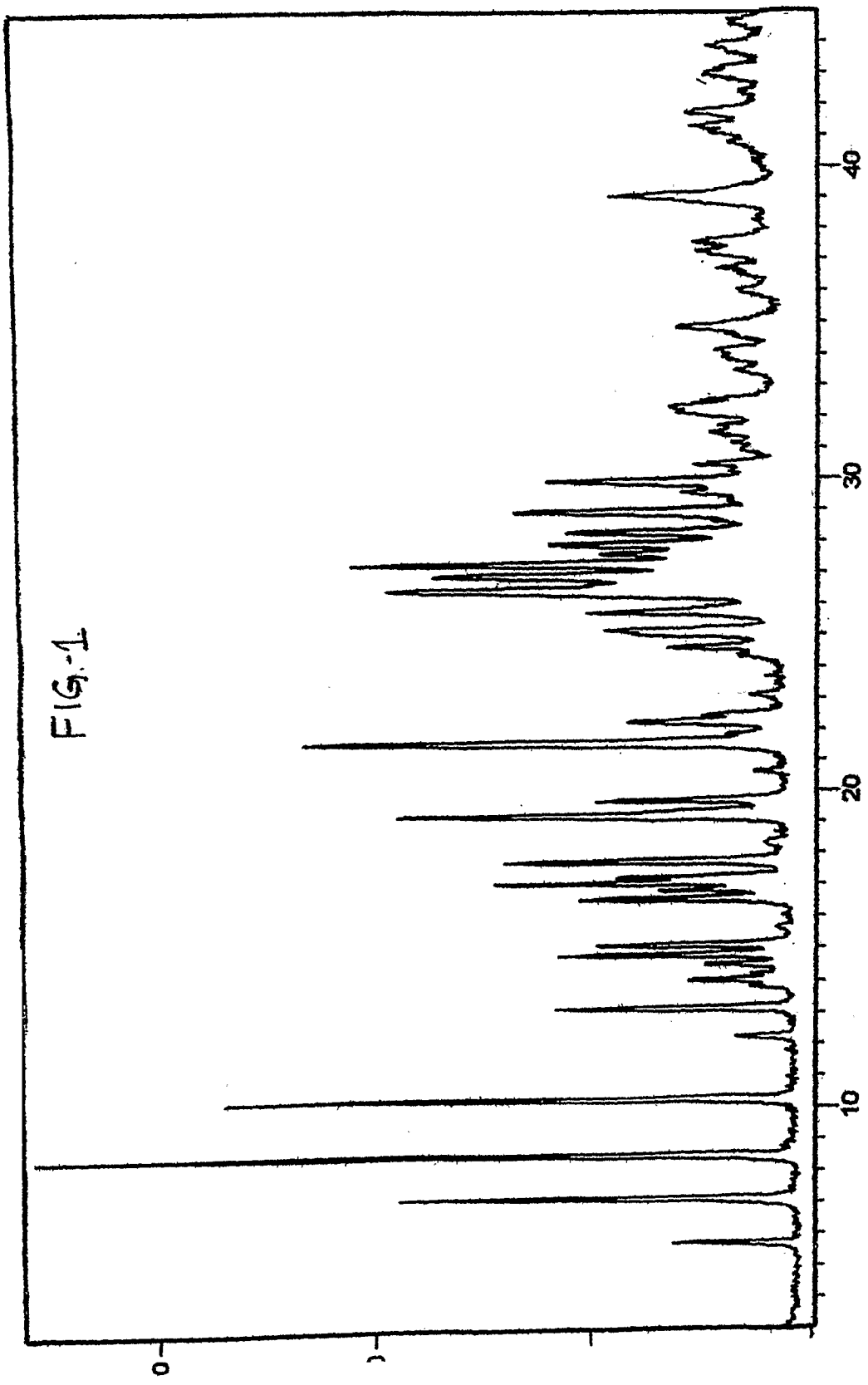
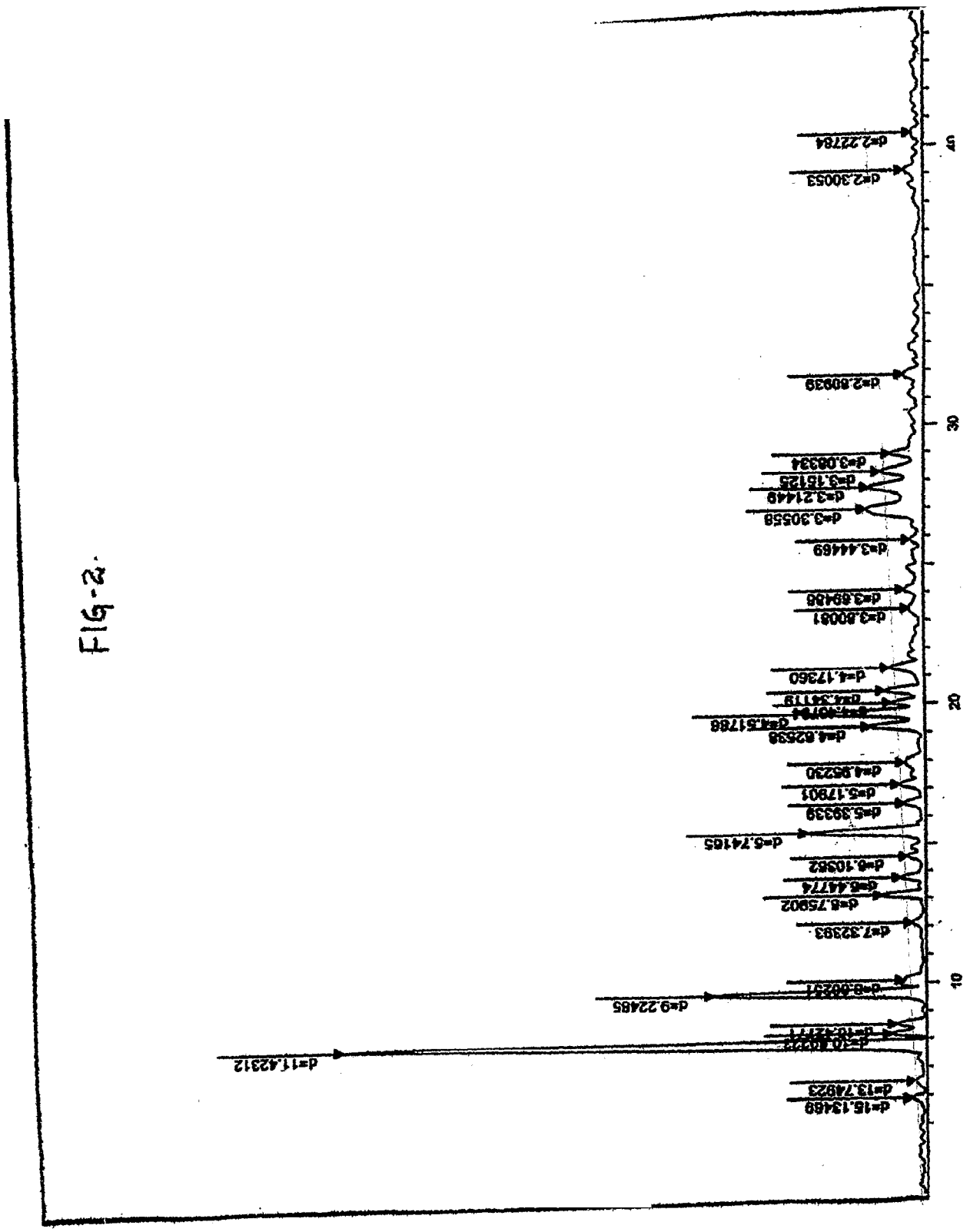


FIG.-1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5
10
20
30

FIG-2.