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(54) Title: DEUCRAVACITINIB AMORPHOUS SOLID DISPERSIONS AND POLYMORPHS THEREOF

(57) Abstract: Disclosed herein is Deucravacitinib amorphous solid dispersions and Polymorphs and to the process for preparation thereof.

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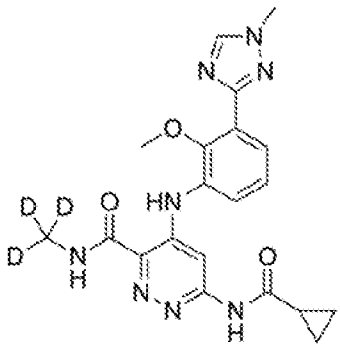
"DEUCRAVACITINIB AMORPHOUS SOLID DISPERSIONS AND POLYMORPHS THEREOF"

FIELD OF THE INVENTION:

The present invention relates to stable Deucravacitinib amorphous solid dispersions and polymorphs and to the process of preparation thereof.

BACKGROUND OF THE INVENTION:

Deucravacitinib (BMS-986165), chemically known as 6-(Cyclopropanecarbonylamido)-4-[2-methoxy-3-(1-methyl-1,2,4-triazol-3-yl)anilino]-N-(trideuteriomethyl)pyridazine-3-carboxamide, is an inhibitor of Tyk2-mediated signal transduction. It selectively binds to the Tyk2 pseudokinase (JH2) domain and blocks receptor-mediated Tyk2 activation by stabilizing the regulatory JH2 domain. The compound is approved for moderate –to-severe plaque psoriasis.



Deucravacitinib was first disclosed in US Patent No. 9505748B2 as amide-substituted heterocyclic compounds useful as modulators of IL-12, IL-23 AND/OR IFN ALPHα responses.

The PCT publications WO2018183656 disclose crystalline Form A of 6-(cyclopropanecarboxamido)-4-((2-methoxy-3-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl) amino)-N-(methyl-d3)pyridazine-3-carboxamide.

WO2019232138 disclose crystalline Form B of 6-(cyclopropanecarboxamido)-4-((2-methoxy-3-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl)amino)-N-(methyl-d3)pyridazine-3-carboxamide wherein the Form B is the HCl salt of a neat crystalline form.

WO2020251911 disclose crystalline salt Forms C and D of 6-(cyclopropanecarboxamido)-4-((2-methoxy-3-(1-methyl-1H-1,2,4- triazol-3-yl) phenyl) amino)-N-(methyl-d 3)pyridazine-3-carboxamide. The Form C is a MSA salt and Form D is a sulfate salt.

WO2021129467 crystalline Forms CSI and CSII of BMS-986165 and a preparation method therefor, a pharmaceutical composition containing the crystal form, and a use of the crystal form in the preparation of a TYK2 inhibitor drug and a drug for treating psoriasis, systemic lupus erythematosus, and Crohn's disease. The X-ray powder diffraction pattern of crystalline Form CSI comprises characteristic peaks at 2theta values of 3.2°±0.2°, 5.6°±0.2° using CuKα radiation. The X-ray powder diffraction pattern of the crystal form CSII has diffraction angle 2θ values of 4.0°±0.2°, 11.4°±0.2°, 13.5°± 0.2°.

WO2021143430 discloses hydrochloride of BMS-986165 characterized by its X-ray powder diffraction pattern having 2θ values of 7.9°±0.2°, 9.4°±0.2°, and 12.5°±0.2.

WO2021143498 disclose a crystal form CSIII of the compound I characteristic peaks at 2θ values of 6.4°±0.2°, 11.3°±0.2°, and 23.2°±0.2°.

WO2021055651 relate to extended-release formulations and dosage forms comprising a dispersion (e.g., spray-dried dispersion) of solid amorphous 6-(cyclopropaneamido)-4-((2-methoxy-3-(1-methyl-1H-1,2,4-triazol-3-yl) phenyl) amino)-N-(methyl-d3)pyridazine-3-carboxamide (Formula (I); BMS-986165) in a

solid polymer matrix for the treatment of auto-immune and auto-inflammatory diseases such as an inflammatory bowel disease (IBD) and psoriasis. The release-controlling polymer is selected from methylcellulose, hydroxypropyl methylcellulose, hydroxypropyl cellulose, carboxymethylcellulose, sodium carboxymethylcellulose, ethyl cellulose, sodium alginate, chitosan, gelatin, tragacanth, xanthan, and mixtures thereof.

WO2022021684 disclose the hydrochloride crystal form CSV of 6-(cyclopropaneamido)-4-((2-methoxy-3-(1-methyl-1H-1,2,4-triazol-3-yl) phenyl) amino)-N-(methyl-d3)pyridazine-3-carboxamide having PXRD peaks at 2θ values of 7.0°±0.2°, 8.9°±0.2°, and 26.0°±0.2°.

WO2022083649 relate to the crystal Form I with the following characteristic peaks: 8.2±0.2°, 11.3±0.2°, 19.3±0.2°, 20.5±0.2° and 23.2° ±0.2°; crystal Form II with characteristic peaks: about 3.3°, about 5.7°, about 8.6°, about 11.8°, about 14.2° and about 18.2°.

WO2022165141 disclose crystalline Form E of 6-(cyclopropanecarboxamido)-4-((2-methoxy-3-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl) amino)-N-(methyl-d3)pyridazine-3-carboxamide characterized by a powder X-ray diffraction pattern comprising two or more 2θ values in degrees (CuKa) selected from: 9.0±0.2, 11.3±0.2, 15.2±0.2, and 21.1±0.2,an endotherm with peak max in the range of from about 249°C to about 253°C.

WO2022212181 provides several crystalline forms of 6-(cyclopropanecarboxamido)-4-((2-methoxy-3-(1-methyl-1H-1,2,4-triazol-3-yl) phenyl) amino)-N-(methyl-d3)pyridazine-3-carboxamide: Form F, Form G, Form H, Form I, Form J, and Form K. Certain of these crystalline forms are hydrates.

WO2022061149 disclose swellable core dosage form comprises a dispersion of amorphous 6-(cyclopropaneamido)-4-((2-methoxy-3-(1-methyl-1H-1,2,4-triazol-3-yl)phenyl)amino)-N-(methyl-d3)pyridazine-3-carboxamide.

A need in the art still exists to provide the compound in its polymorph forms and as amorphous solid dispersion which is physically and chemically stable at storage conditions and has sufficient solubility and bioavailability thereby reducing the dosages.

The present inventors surprisingly found that it is possible to provide polymorphic forms of the compound and improved amorphous solid dispersions with improved physical and pharmacological activity and to the process of preparation thereof. This remains the object of the invention.

SUMMARY OF THE INVENTION

In accordance with the above, the present invention provides Deucravacitinib amorphous solid dispersions and polymorphs which are physically and chemically stable at storage conditions and has sufficient solubility and bioavailability and to the process for preparation thereof.

In an aspect, the present invention provides Deucravacitinib polymorph Form C2 characterized by PXRD peaks, DSC and TGA as shown in Fig 1(a-c) and Fig 2(a-c) respectively and to the process for preparation thereof.

In another aspect, the present invention provides Deucravacitinib polymorph Form C3 characterized by PXRD peaks as shown in Fig 3 and to the process for preparation thereof.

In yet another aspect, the present invention provides Deucravacitinib polymorph Form C4 characterized by PXRD peaks as shown in Fig 4 and to the process for preparation thereof.

In another aspect, the present invention provides Deucravacitinib polymorph Form C5 characterized by PXRD peaks as shown in Fig 5 and to the process for preparation thereof.

In yet another aspect, the present invention provides a process for preparation of polymorphic forms C2, C3, C4 and C5 of Deucravacitinib comprising;

a) Dissolving Deucravacitinib base in the solvent selected from alcohols, substituted alcohols, ethers, halogenated hydrocarbons, aliphatic or aromatic hydrocarbons, ethers, ketones, nitriles, acids, carbonates and carbonate esters and the like alone or mixtures thereof to obtain a clear solution;
b) Stirring the clarified solution in a pre-chilled solvent selected from lower alcohols, ethers, halogenated hydrocarbons, ethers, ketones, aliphatic or aromatic hydrocarbons and the like alone or mixtures thereof; and
c) Filtering and drying under vacuum to obtain the desired polymorphs.

In an aspect, the solvents for preparation of Deucravacitinib polymorphs C2, C3, C4 and C5 is selected from alcohols, substituted alcohols, ethers, halogenated hydrocarbons, aliphatic or aromatic hydrocarbons, ketones, nitriles, acids, carbonates and carbonate esters and the like alone or in combination thereof.

In a preferred aspect, the present invention provides stable amorphous solid dispersions of Deucravacitinib with dispersing agents selected from the polymers such as PVP K30, Kollidon® VA 64, Eudragit L100; Eudragit L100 55, HPMC Phthalate (HPMC HP 55) and the like alone or mixtures thereof.

The process for preparation of amorphous solid dispersions of Deucravacitinib comprises;

a) Dissolving crystalline Deucravacitinib and the dispersing agent selected from PVP K30, Kollidon® VA 64, Eudragit L100, Eudragit L100 55, HPMC Phthalate (HPMC HP 55) and the like alone or mixtures thereof in the solvent at ambient temperature till a clear particle free solution is obtained; and

b) Subjecting the filtrate to distillation under vacuum followed by drying to obtain the desired product.

In an aspect, the process step (b) comprises a step of spray drying prior to vacuum drying to obtain amorphous solid dispersion of Deucravacitinib with HPMC HP 55 or Eudragit L100 55.

In another aspect, the present invention provides Deucravacitinib amorphous solid dispersion with PVP K30 characterized by PXRD and DSC depicted in Fig 6a and 6b respectively.

In yet another aspect, the present invention provide Deucravacitinib amorphous solid dispersion with Kollidon® VA 64 characterized by PXRD and DSC depicted in Fig 7a and 7b respectively.

In another aspect, the present invention provides Deucravacitinib amorphous solid dispersion with Eudragit L100 characterized by PXRD and DSC depicted in Fig 8a and 8b respectively.

In another aspect, the present invention provides Deucravacitinib amorphous solid dispersion with Eudragit L100 55 characterized by PXRD and DSC depicted in Fig 9a and 9b respectively.

In yet another aspect, the present invention provides Deucravacitinib amorphous solid dispersion with HPMC HP 55 characterized by PXRD and DSC depicted in Fig 10a and 10b respectively.

DESCRIPTION OF THE FIGURES

Fig 1: depict (a) PXRD of Deucravacitinib Form C2; (b) DSC of Deucravacitinib Form C2 and (c) TGA of Deucravacitinib Form C2 obtained as per the process of example 1a.

Fig 2: depict (a) PXRD of Deucravacitinib Form C2; (b) DSC of Deucravacitinib Form C2 and (c) TGA of Deucravacitinib Form C2 obtained as per the process of example 1b.

Fig 3: depict PXRD of Deucravacitinib Form C3 obtained as per the example 2

Fig 4: depict PXRD of Deucravacitinib Form C4 obtained as per the example 3

Fig 5: depict PXRD of Deucravacitinib Form C4 obtained as per the example 4

Fig 6: depict (a) depict PXRD and (b) mDSC of Deucravacitinib Amorphous solid dispersion with PVP K30 obtained as per the example 5

Fig 7: depict (a) PXRD and (b) mDSC of Deucravacitinib Amorphous solid dispersion with Kollidon® VA64 obtained as per the example 6

Fig 8: depict (a) PXRD and (b) mDSC of Deucravacitinib Amorphous solid dispersion with Eudragit L100 obtained as per the example 7.

Fig 9: depict (a) PXRD and (b) mDSC of Deucravacitinib Amorphous solid dispersion with Eudragit L100 55 obtained as per the example 9.

Fig 10: depict (a) PXRD and (b) mDSC of Deucravacitinib Amorphous solid dispersion with HPMC HP 55 obtained as per the example 8.

DETAILED DESCRIPTION OF THE INVENTION

The present invention will now be explained in detail with reference to its various preferred as well as optional embodiment, which, however should not be construed to limit the scope of the invention.

The present invention relates to Deucravacitinib amorphous solid dispersions and polymorphs thereof which are physically and chemically stable at storage conditions and has sufficient solubility and bioavailability and to the process for preparation thereof.

In an embodiment, the present invention relates to Deucravacitinib polymorph Form C2 characterized by PXRD peaks, DSC and TGA as shown in Fig 1(a-c) and Fig 2(a-c) respectively and to the process for preparation thereof.

In another embodiment, the present invention discloses Deucravacitinib polymorph Form C3 characterized by PXRD peaks as shown in Fig 3 and to the process for preparation thereof.

In yet another embodiment, the present invention disclose Deucravacitinib polymorph Form C4 characterized by PXRD peaks as shown in Fig 4 and to the process for preparation thereof.

In yet another embodiment, the present invention discloses Deucravacitinib polymorph Form C5 characterized by PXRD peaks as shown in Fig 5 and to the process for preparation thereof.

In an embodiment, the present invention relates to preparation of Deucravacitinib polymorphic Forms C2, C3, C4 and C5 which comprises dissolving Deucravacitinib base in the solvent selected from alcohols, substituted alcohols, ethers, halogenated hydrocarbons, aliphatic or aromatic hydrocarbons, ethers, ketones, nitriles, acids, carbonates and carbonate esters and the like alone or in combination thereof to obtain a clear solution. Stirring the clarified solution in a pre-chilled solvent selected from lower alcohols, ethers, halogenated hydrocarbons, ethers, ketones, aliphatic or aromatic hydrocarbons and the like alone or in combination thereof, filtering and drying under vacuum to obtain the desired compound.

Accordingly, the present invention disclose preparation of Deucravacitinib polymorphic Form C2 from lower alcohol, halogenated hydrocarbon alone or in combination thereof characterized by PXRD peaks at 6.99, 7.7, 9.1, 11.45, 17.34, 18.4, 19.01 and 22.60 ±2θ and by DSC and TGA depicted in Fig 1(a-c) and Fig

2(a-c) respectively. Particularly, the solvents are selected from chloroform, methanol, methylene dichloride, 1,2 dichloroethane alone or mixtures thereof.

In another embodiment, the present invention relate to preparation of Deucravacitinib polymorphic Form C3 from nitriles, acids and ethers alone or in combination thereof characterized by PXRD peaks at 6.57, 7.75, 8.61, 9.43, 15.6, 24.09, 25.29, 26.46, 27.06 ±2θ depicted in Fig 3. Particularly, the solvents are selected from methyl tertiary butyl ether, acetonitrile, formic acid alone or mixtures thereof.

In another embodiment, the present invention relate to preparation of Deucravacitinib polymorphic Form C4 from lower alcohols, acids and ethers alone or in combination thereof characterized by PXRD peaks at 7.09, 9.18, 14.22, 18.86, 20.04 ±2θ depicted in Fig 4. Particularly, the solvents are selected from Diisopropyl ether, Ethanol, Acetic acid, alone or mixtures thereof.

In yet another embodiment, the present invention disclose preparation of Deucravacitinib polymorphic Form C5 from alcohols, substituted alcohols, carbonates and carbonate esters alone or in combination thereof characterized by PXRD peaks at 10.14, 14.41, 14.96, 18.98 and 21.50 depicted in Fig 5. Particularly, the solvents are elected from Trifluoroethanol.

In a preferred embodiment, the present invention relates to a stable amorphous solid dispersions of Deucravacitinib with dispersing agents selected from the polymers such as PVP K30, Kollidon® VA 64, Eudragit L100; Eudragit L100 55, HPMC Phthalate (HPMC HP 55) and the like alone or mixtures thereof.

In an embodiment, the present invention relate to Deucravacitinib amorphous solid dispersion with PVP K30 characterized by PXRD and DSC depicted in Fig 6a and 6b respectively.

In yet another aspect, the present invention disclose Deucravacitinib amorphous solid dispersion with Kollidon® VA 64 characterized by PXRD and DSC depicted in Fig 7a and 7b respectively.

In another aspect, the present invention relates to Deucravacitinib amorphous solid dispersion with Eudragit L100 characterized by PXRD and DSC depicted in Fig 8a and 8b respectively.

In another embodiment, the present invention discloses Deucravacitinib amorphous solid dispersion with Eudragit L100 55 characterized by PXRD and DSC depicted in Fig 9a and 9b respectively.

In yet another embodiment, the present invention relates to Deucravacitinib amorphous solid dispersion with HPMC HP 55 characterized by PXRD and DSC depicted in Fig 10a and 10b respectively.

In another embodiment, the present invention disclose process for preparation of Deucravacitinib amorphous solid dispersions with dispersing agents selected from the polymers such as PVP K30, Kollidon® VA 64, Eudragit L100, Eudragit L100 55, HPMC HP 55 and the like alone or in combination thereof. Accordingly, crystalline Deucravacitinib and the dispersing agent are dissolved in the solvent selected from lower alcohol, halogenated hydrocarbon and the like alone or in combination thereof at ambient temperature till a clear particle free solution is obtained. The clear filtrate is then optionally spray dried, subjected to distillation under vacuum followed by drying to obtain the desired product.

Accordingly, the process for preparation of amorphous solid dispersions of Deucravacitinib comprises;

a) Dissolving crystalline Deucravacitinib and the dispersing agent selected from PVP K30, Kollidon® VA 64, Eudragit L100, Eudragit L100 55, HPMC Phthalate (HPMC HP 55) and the like alone or

mixtures thereof in the solvent at ambient temperature till a clear particle free solution is obtained; and

b) Subjecting the filtrate to distillation under vacuum followed by drying to obtain the desired product.

In an embodiment, the process step (b) comprises a step of spray drying prior to vacuum drying to obtain amorphous solid dispersion of Deucravacitinib with HPMC HP 55 or Eudragit L100 55.

In yet another embodiment, the present invention relates to pharmaceutical composition containing Deucravacitinib polymorphic forms C2, C3, C4 or C5 of the present invention together with pharmaceutically acceptable excipients.

Each of the polymorphic forms of Deucravacitinib described herein may be used alone or in combination with other polymorphic forms of Deucravacitinib described herein and/or formulated with one or more excipients or other active pharmaceutical ingredients to make pharmaceutical compositions.

The pharmaceutical composition of the stable polymorphic forms C2 C3, C4 or C5 of the present invention may be formulated in oral, liquid or parenteral form and may be administered to a subject in need thereof in therapeutically effective amount.

In another embodiment, the present invention relate to pharmaceutical composition containing Deucravacitinib amorphous solid dispersion PVP K30, Kollidon® VA 64, Eudragit L100, Eudragit L100 55 or HPMC HP 55 of the present invention together with pharmaceutically acceptable excipients.

The pharmaceutical composition of the stable solid dispersions of amorphous Deucravacitinib PVP K30, Kollidon® VA 64, Eudragit L100, Eudragit L100 55

or HPMC HP 55 may be formulated in oral, liquid or parenteral form and may be administered to a subject in need thereof in therapeutically effective amount.

Examples:

The invention will now be further described by the following working example(s), which are preferred embodiments of the invention. All temperatures are in degrees Celsius (°C) unless otherwise indicated. These examples are illustrative rather than limiting and it is to be understood that there may be other embodiments that fall within the spirit and scope of the invention appended hereto.

Example 1a: Preparation of Deucravacitinib polymorph Form C2

Dissolved 5.0 gm of Deucravactitinib in 100 ml of chloroform and 10 ml of Methanol at 30° C and the solution was clarified. The resulted clear solution is subjected to vacuum distillation at 50 °C using Buchi rotavapor. After complete distillation collected the material and charged into pre chilled methylene dichloride at -15°C and stirred the reaction mass at this temperature for 3-5 hrs. The resulted material is filtered and suck dried under vacuum for 30 min, then further dried at 40 °C in Air tray dryer (ATD) for 6 hrs, then at 80 °C for 12 hr to get the titled compound.

Yield: 3.8gm

Example 1b:

Dissolved 0.5 gm of Deucravactitinib in 10 ml of chloroform and 1.0 ml of Methanol at 30 ° C and the solution was clarified. The resulted clear solution is subjected to vacuum distillation using Buchi rotavapor. After complete distillation frothing type material is obtained, collected the material and charged in to 5 ml of pre chilled 1,2 dichloroethane at -10 °C and stirred the reaction mass at this temperature for 3-5 hrs. The resulted material is filtered and suck dried under vacuum for 30 min, then further dried at 40 °C under vacuum for 2-3 hrs to get the titled compound.

Yield: 0.3gm

Example 2: Preparation of Deucravacitinib polymorph Form C3

Charged 125 ml of methyl tertiary butyl ether (MTBE) in a clean RBF and cooled it to -10 to -15°C. Dissolved separately 5g of Deucravacitinib in a solvent mixture comprising acetonitrile (30 ml), formic acid (10 ml) and the solution was clarified. Charged this clarified solution into above pre chilled MTBE and the reaction mass is stirred for 4 to 5 hrs. Filtered the solids and the material dried in vacuum tray drier for 2-3 hrs at 40°C and 4 -5 hrs at 50°C to obtain the title compound.

Yield: 4.6 gm

Example 3: Preparation of Deucravacitinib polymorph Form C4

Charged 5 ml of Diisopropyl ether (DIPE) in a clean RBF and cooled it to -10 to -15°C. Dissolved separately 0.5g of Deucravacitinib in a solvent mixture comprising Ethanol (2 ml), Acetic acid (1 ml) and the solution was clarified. Charged this clarified solution into above pre chilled DIPE and the reaction mass was stirred for 4 to 5 hrs at -10 to -15°C.Added another 5ml of DIPE and stirred for 10min at -10 to -15°C Filtered the solids and the material was dried in vacuum tray drier for 2-3 hrs at 40°C and 2-3 hrs at 60°C to obtain the title compound.

Yield: 0.2 gm

Example 4: Preparation of Deucravacitinib polymorph Form C5

Dissolved 2.0 gm of Deucravactitinib in 10 ml of Trifluoroethanol at 30 °C and the solution was clarified. The resulted clear solution was added to 30 ml of Dimethyl carbonate for about 3-5min at 20-25°C and cooled the reaction mass to 0-5°C and stirred for 1-2 hrs at 0 -5°C. Filtered the material and dried at 45°C in Air tray drier(ATD) for 2-3 hrs to obtain the title compound.

Yield: 1.8 gm

Example 5: Preparation Amorphous solid dispersions of Deucravactitinib with PVP K30

Dissolved 1gm of Deucravacitinib and 3gm of PVP K30 in 20ml methylene dichloride (MDC) and 2ml of Methanol at 30°C and the solution was clarified. The clear filtrate subjected to distillation at 45°C under vacuum by using rotary evaporator, after complete distillation, collected the material and further dried at 45°C under vacuum for 8 hr to obtain 2.6 gm of the title compound.

Yield: 2.6gm

Example 6: Preparation Amorphous solid dispersions of Deucravactitinib with Kollidon® VA 64

Dissolved 1gm of Deucravacitinib and 3gm of Kollidon® VA 64 in 20 ml MDC and 2 ml of Methanol at 30°C and the solution was clarified. The clear filtrate subjected to distillation at 45 °C under vacuum by using rotary evaporator, after complete distillation, collected the material and further dried at 45° C under vacuum for 8 hr to obtain the title compound.

Yield: 3.0gm

Example 7: Preparation Amorphous solid dispersions of Deucravactitinib with Eudragit L100

Dissolved 1 gm of Deucravacitinib and 3 gm of Eudragit L100 in 50 ml MDC and 10 ml of Methanol at 30°C and the solution was clarified. The clear filtrate subjected to distillation at 45 °C under vacuum by using rotary evaporator, after complete distillation, collected the material and further dried at 45° C under vacuum for 2 hr to obtain the title compound.

Yield: 3.0gm

Example 8: Preparation Amorphous solid dispersions of Deucravactitinib with Eudragit L100 55

Dissolved Deucravacitinib (15.0 g) and Eudragit L100-55 (85.0 g) in a mixture of Methanol (1250ml) and Acetone (1250.0 ml) at 55-60 °C and the solution was clarified by removing any undissolved particulate. The clear solution was

subjected to spray-drying followed by drying at 40 °C in vaccumfor 30-35 hrs to yield Amorphous solid dispersion of Deucravacitinib with Eudragit L100-55.
Yield: ~80 gm

Example 9: **Preparation Amorphous solid dispersions of Deucravactitinib with HPMC HP 55**
Dissolved Deucravacitinib (15.0 g) and HPMC HP 55 (85.0 g) in a mixture of Methanol (750ml) and MDC (750.0 ml) at 40-50°C and the solution was clarified by removing any undissolved particulate. The clear solution was subjected to spray-drying followed by drying at 45°C in vacuum for 30-40 hrs to yield Amorphous solid dispersion of Deucravacitinib with HPMC HP 55.
Yield: ~80 gm

Although the invention has been described in detail in the foregoing for the purpose of illustration, it is to be understood that such detail is solely for that purpose and that variations can be made therein by those skilled in the art without departing from the spirit and scope of the invention except as it may be limited by the claims.

We Claim;

1. A stable amorphous solid dispersions of Deucravacitinib with the dispersing agent selected from PVP K30, Kollidon® VA 64, Eudragit L100, Eudragit L100-55, HPMC Phthalate (HPMC HP 55) and the like alone or mixtures thereof.

2. The amorphous solid dispersion of Deucravacitinib as claimed in claim 1, wherein the solid dispersion of Deucravacitinib with PVPK30 characterized by mDSC at about 137± 3°C.

3. The amorphous solid dispersion of Deucravacitinib as claimed in claim 1, wherein the solid dispersion of Deucravacitinib with Kollidon® VA 64 characterized by mDSC at about 101±3°C .

4. The amorphous solid dispersion of Deucravacitinib as claimed in claim 1, wherein the solid dispersion of Deucravacitinib with Eudragit L100 characterized by mDSC at about 174 ± 3°C.

5. The amorphous solid dispersion of Deucravacitinib as claimed in claim 1, wherein the solid dispersion of Deucravacitinib with Eudragit L100-55 characterized by mDSC at about 121±3°C.

6. The amorphous solid dispersion of Deucravacitinib as claimed in claim 1, wherein the solid dispersion of Deucravacitinib with HPMC HP 55 characterized by mDSC at about 126±3°C.

7. A process for preparation of stable amorphous solid dispersion of Deucravacitinib as claimed 1 comprising;
    a) Dissolving crystalline Deucravacitinib and the dispersing agent selected from PVP K30, Kollidon® VA 64, Eudragit L100, Eudragit L100-55, HPMC Phthalate (HPMC HP 55) and the like

alone or mixtures thereof in the solvent till a clear particle free solution is obtained;

b) Subjecting the filtrate to distillation under vacuum followed by drying to obtain the desired product.

8. The process as claimed in claim 7, wherein step (b) optionally comprises the step of spray drying prior to vacuum drying to obtain amorphous solid dispersion of Deucravacitinib with HPMC HP 55 or Eudragit L100 55.

9. A pharmaceutical composition comprising solid dispersions of Deucravacitinib as claimed in claim any one of the preceding claims together with pharmaceutically acceptable excipients.

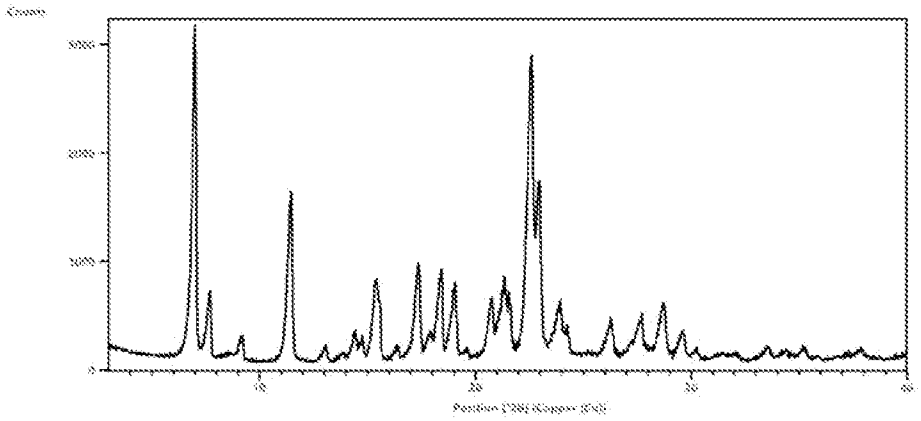


Fig 1a

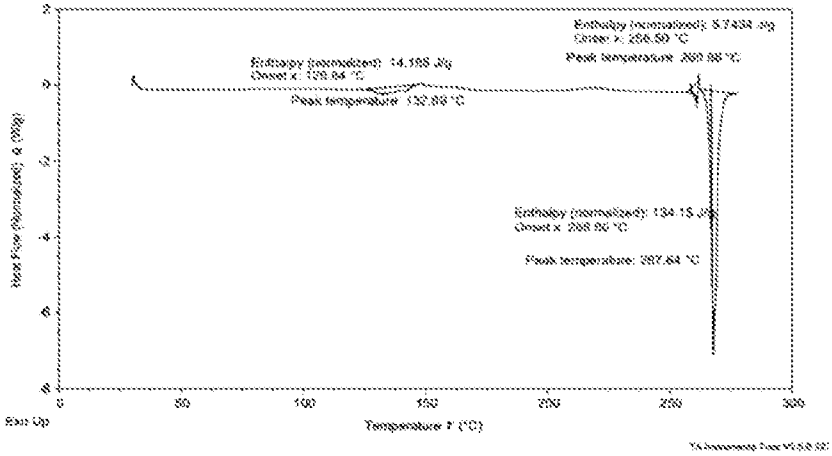


Fig 1b

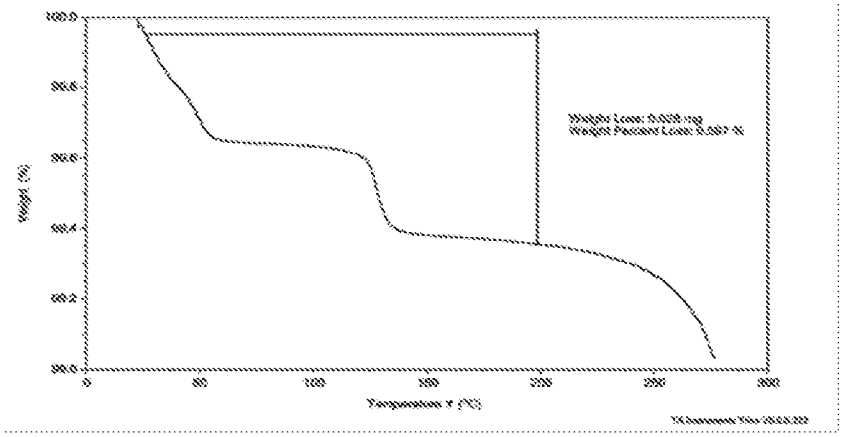


Fig 1c

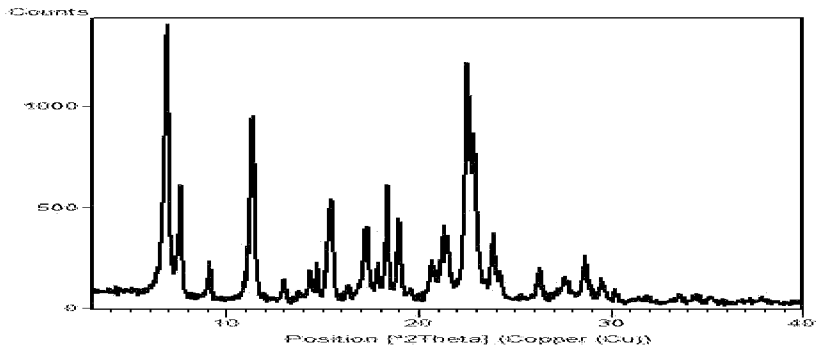


Fig 2a

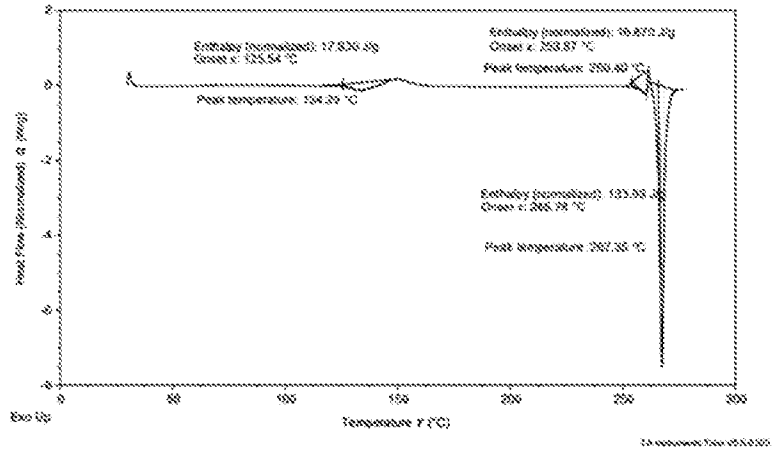


Fig 2b

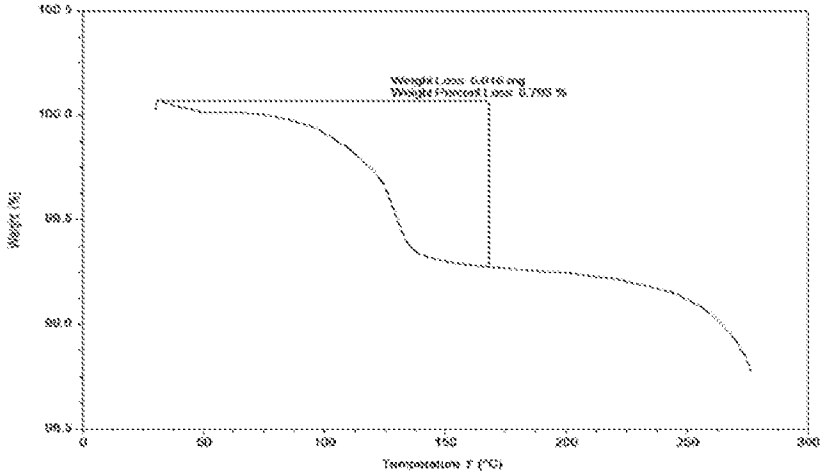


Fig 2c

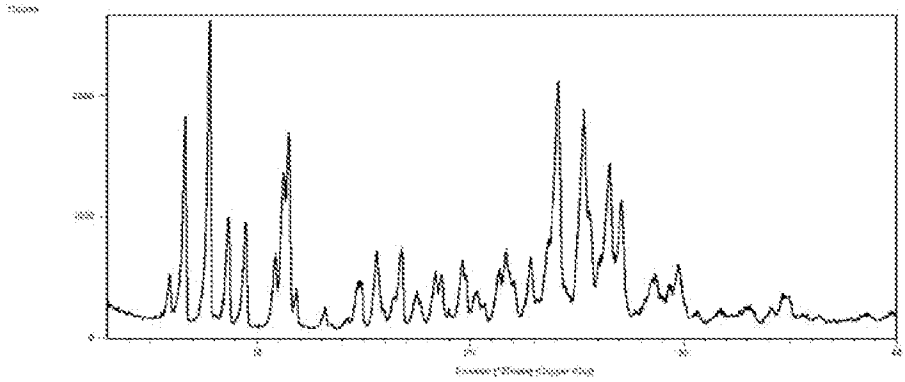


Fig 3

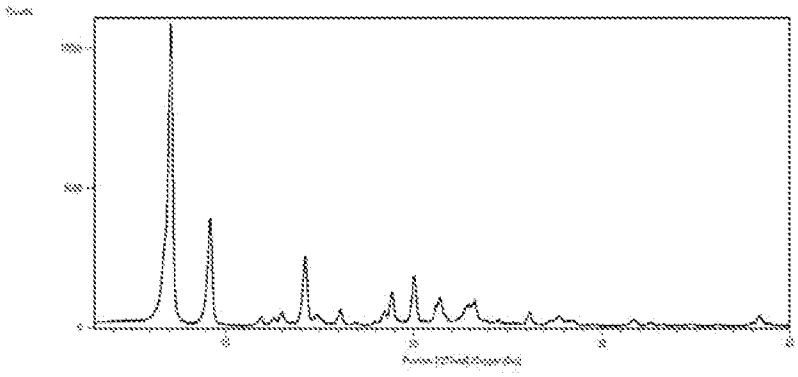


Fig 4

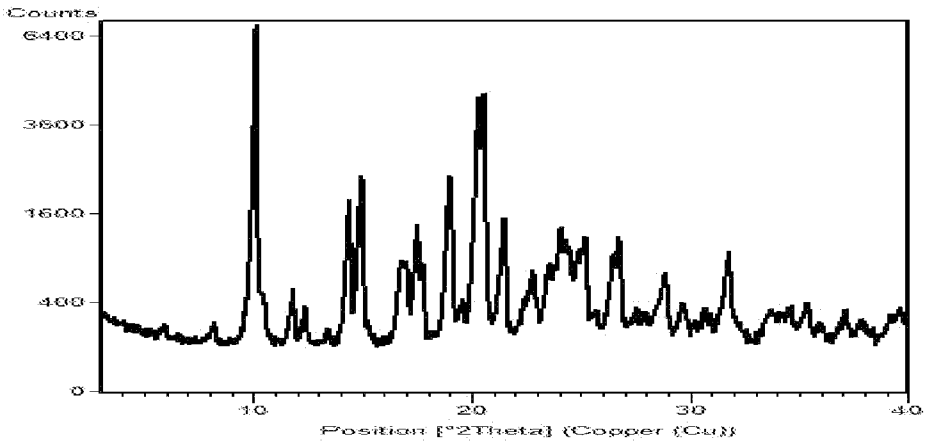

Counts
6400
3600
1600
400
0
10
20
30
40
Position [°2Theta] (Copper (Cu))

Fig 5

VI/X

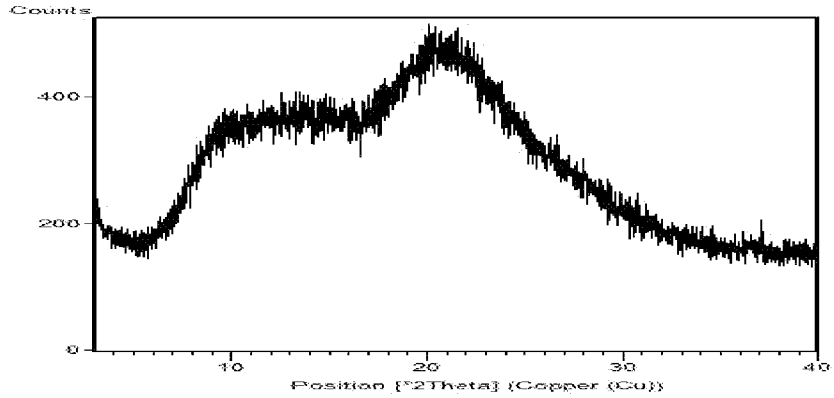


Fig 6a

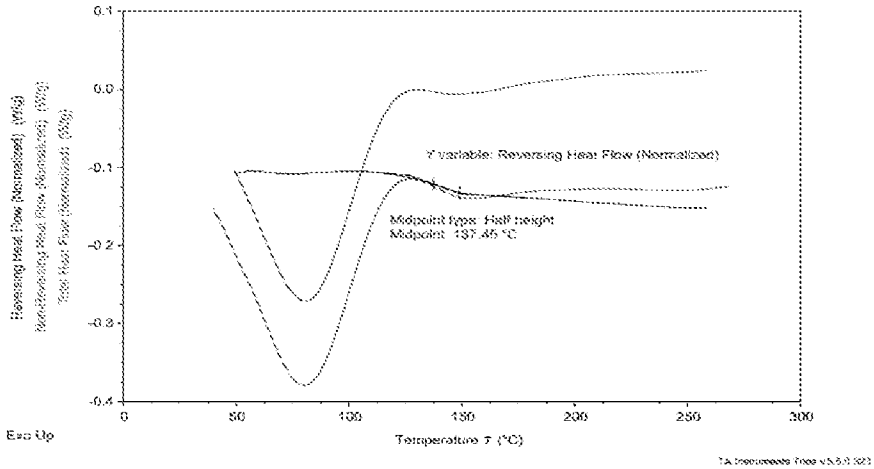


Fig 6b

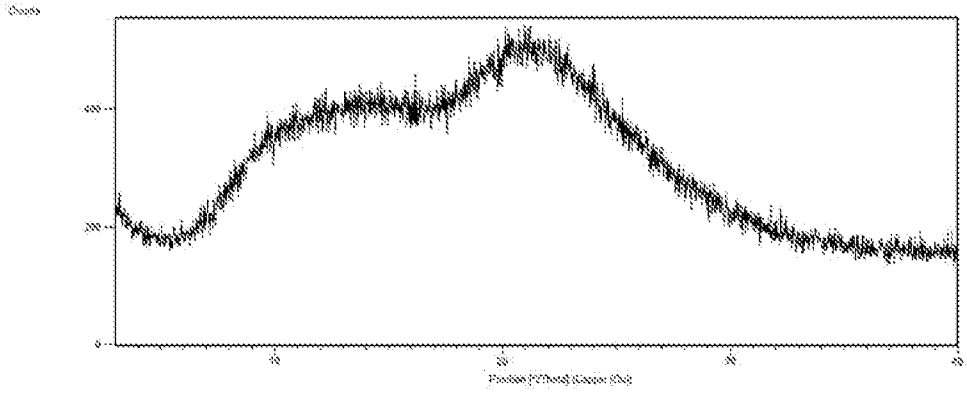


Fig 7a

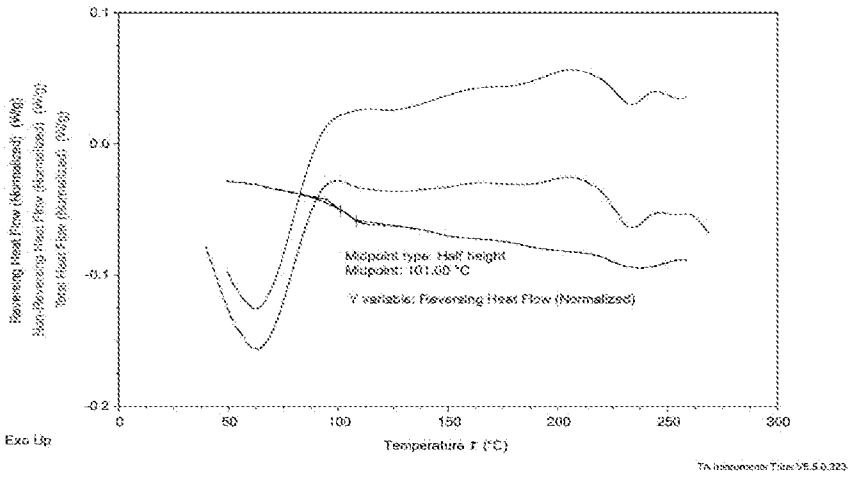

Midpoint type: Half height
Midpoint: 101.68 °C
Y variable: Reversing Heat Flow (Normalized)
Exo Up
Temperature T (°C)

Fig 7b

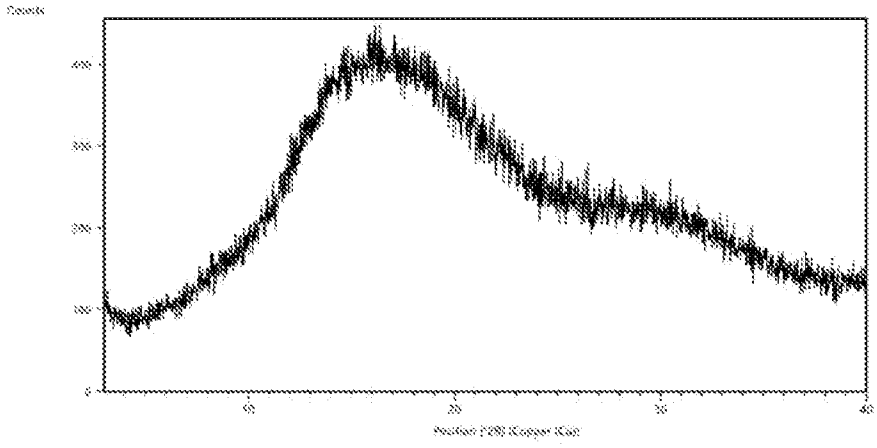


Fig 8a

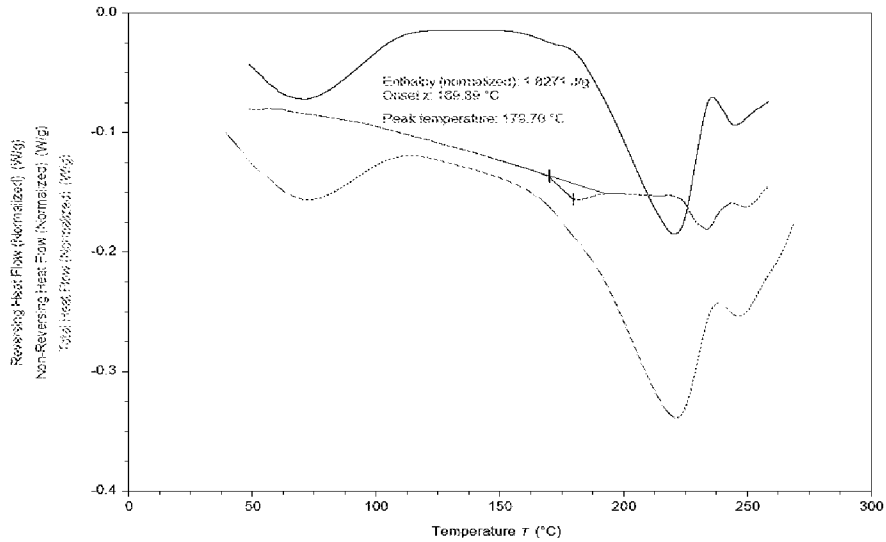

0.0
-0.1
-0.2
-0.3
-0.4
0
50
100
150
200
250
300
Temperature T (°C)
Peak temperature: 179.76 °C

Fig 8b

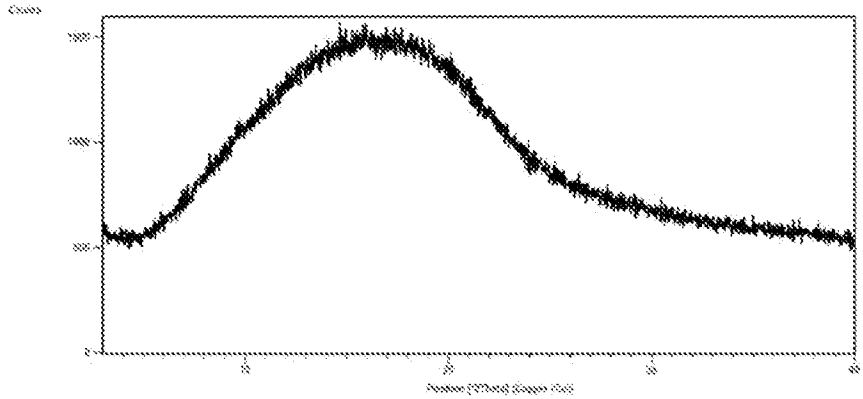


Fig 9a

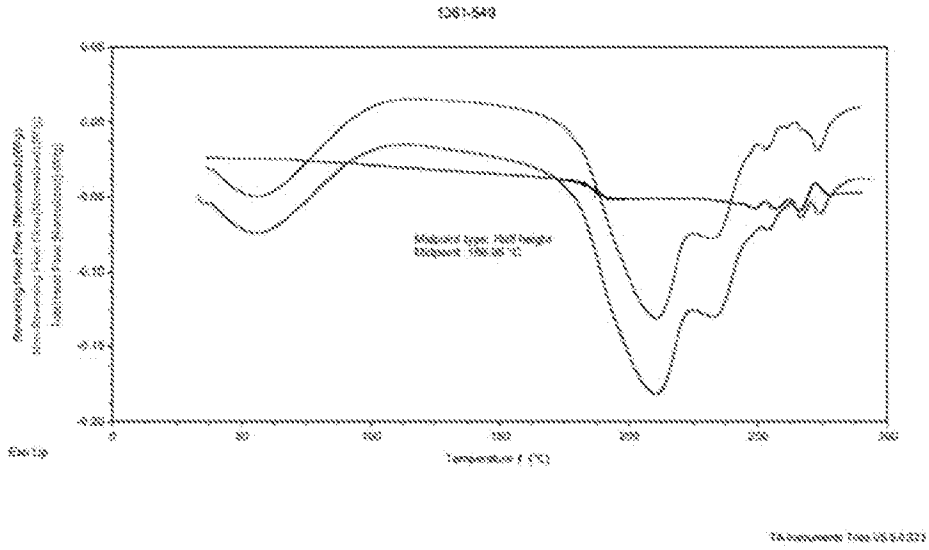


Fig 9b

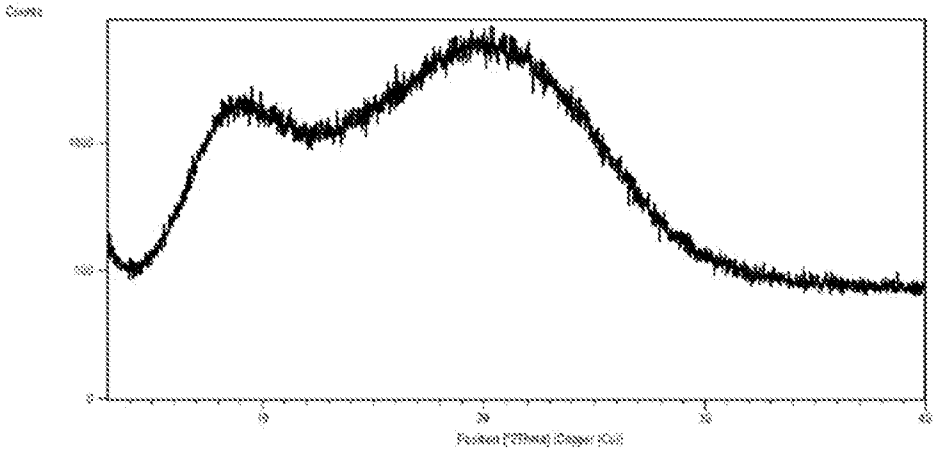


Fig 10(a)

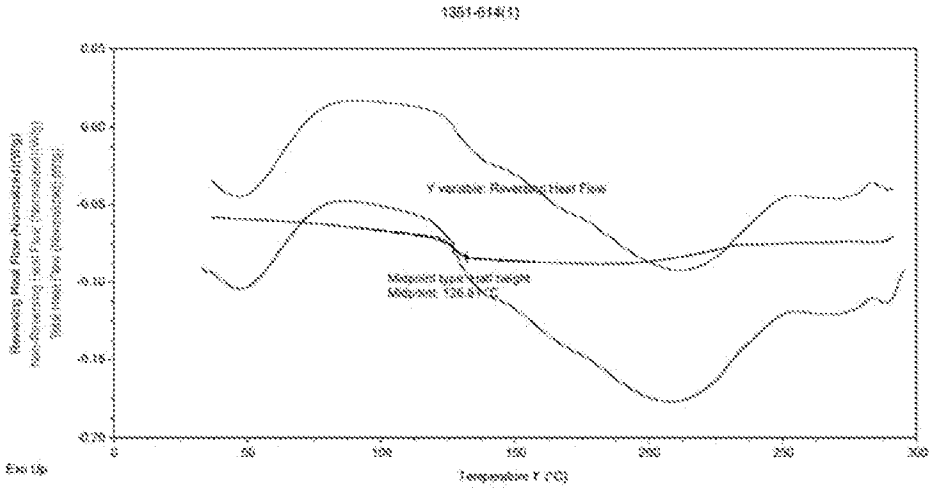


Fig 10b

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN2024/050192

A. CLASSIFICATION OF SUBJECT MATTER
A61K31/501,C07D403/12 Version=2024.01

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61K, C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database consulted during the international search (name of database and, where practicable, search terms used)

PatSeer, IPO Internal Database

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
PX	WO2023181075A1 (DR REDDYS LABORATORIES LTD) 28 SEPTEMBER 2023 (28.09.2023); abstract, discription, claims 1-12. [FAMILY: NONE]	1-9
X	WO2021055651A1(BRISTOL MYERS SQUIBB CO) 25 MARCH 2021 (25.03.2021); abstract, page no. 4 para. 2, page no. 7 para. 2-3, page no. 10, para. 4, claims 1-6.	1-9
Y	WO2021239893A1 (BEND RES INC [US]; LONZA AG) 02 DECEMBER 2021 (02.12.2021); abstract, page no. 16 para. 3, Fig. 9, claims 1-20. [FAMILY: NONE]	1-9
Y	WO2021143498A1 (CRYSTAL PHARMACEUTICAL SUZHOU CO LTD) 22 JULY 2021 (22.07.2021); abstract, Fig. 2-3, Example 3, claim 6	1-9

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10-05-2024	10-05-2024

Name and mailing address of the ISA/	Authorized officer
Indian Patent Office Plot No.32, Sector 14,Dwarka,New Delhi-110075 Facsimile No.	Himanshu Singh Telephone No. +91-1125300200

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IN2024/050192

Citation	Pub.Date	Family	Pub.Date
WO 2021055651 A1	25-03-2021	CN 114727948 A	08-07-2022
		EP 4031109 A1	27-07-2022
		JP 2022548687 A	21-11-2022
		KR 20220066310 A	24-05-2022
		US 2023255964 A1	17-08-2023
WO 2021143498 A1	22-07-2021	CN 114787154 A	22-07-2022
		US 2023049130 A1	16-02-2023