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(54) **Title**: SAXAGLIPTIN HYDROCHLORIDE SOLID DISPERSION

(57) **Abstract**: The present invention provides a novel amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier, process for its preparation and pharmaceutical compositions comprising it.

SAXAGLIPTIN HYDROCHLORIDE SOLID DISPERSION

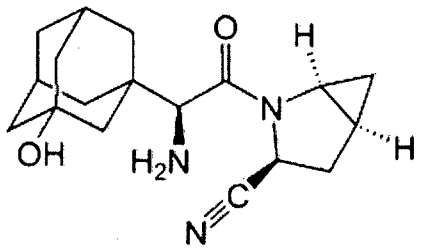
This application claims the benefit of Indian Provisional Patent Application No. 5537/CHE/2012, filed on December 31, 2012, which is incorporated herein by reference.

Filed of the Invention

The present invention provides a novel amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier, process for its preparation and pharmaceutical compositions comprising it.

Background of the Invention

Saxagliptin, chemically (1*S*,3*S*,5*S*)-2-[(2*S*)-2-amino-2-(3-hydroxy-1-adamantyl) acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile and has the structure formula:



Saxagliptin hydrochloride is a new oral hypoglycemic (anti-diabetic drug) of the new dipeptidyl peptidase-4 (DPP-4) inhibitor class of drugs. The generic name saxagliptin hydrochloride is marketed by BRISTOL MYERS SQUIBB under the brand name Onglyza®.

Saxagliptin and its process were disclosed in U.S. Patent No. 6,395,767.

U.S. patent no. 7,420,079 described saxagliptin hydrochloride and its process.

Polymorphism is defined as "the ability of a substance to exist as two or more crystalline phases that have different arrangement and/or conformations of the molecules in the crystal Lattice. Thus, in the strict sense, polymorphs are different crystalline structures of the same pure substance in which the molecules have different arrangements and/or different configurations of the molecules". Different polymorphs may differ in their physical properties such as melting point, solubility, X-ray diffraction patterns, etc.

Although those differences disappear once the compound is dissolved, they can appreciably influence pharmaceutically relevant properties of the solid form, such as handling properties, dissolution rate and stability. Such properties can significantly influence the processing, shelf life, and commercial acceptance of a polymorph. It is therefore important to investigate all solid forms of a drug, including all polymorphic forms, and to determine the stability, dissolution and flow properties of each polymorphic form. Polymorphic forms of a compound can be distinguished in the laboratory by analytical methods such as X-ray diffraction (XRD), Differential Scanning Calorimetry (DSC) and Infrared spectrometry (IR).

Solvent medium and mode of crystallization play very important role in obtaining one polymorphic Form over the other.

Saxagliptin and its hydrochloride can exist in different polymorphic Forms, which may differ from each other in terms of stability, physical properties, spectral data and methods of preparation.

U.S. patent no. 7,943,656 disclosed crystalline Form H2-1 (1HCl), Form H0.75-3, Form H1.67-1, Form H2-1 (2HCl) and Form P-5 of saxagliptin hydrochloride.

International patent application publication no. WO 2010/115974 disclosed crystalline Form 1-S, Form HT-S, Form HT-IV-S and Form IV-S of saxagliptin hydrochloride.

International patent application publication no. WO 2012/047871 disclosed crystalline Form K, Form T, Form Z, Form N, Form S, Form O, Form B, Form C, Form D, Form H1.25-2 and amorphous Form of saxagliptin hydrochloride.

It was observed that the crystalline Forms and amorphous Form of saxagliptin hydrochloride either not reproducible or not stable.

We have also found a novel amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier. The amorphous solid dispersion of saxagliptin hydrochloride is stable, reproducible and so, the amorphous solid dispersion of saxagliptin hydrochloride is suitable for formulating saxagliptin hydrochloride. Normally amorphous Forms are hygroscopic. Amorphous solid dispersion of saxagliptin hydrochloride is found to be non-hygroscopic.

Thus, an object of the present invention is to provide a novel amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier, process for its preparation and pharmaceutical compositions comprising it.

Summary of the Invention

In one aspect, the present invention provides amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier.

In another aspect, the present invention there is provided a process for the preparation of amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier, which comprises:

a) preparing a solution comprising a mixture of saxagliptin hydrochloride and one or more pharmaceutically acceptable carriers selected from copovidone, ethyl cellulose, hydroxypropyl methylcellulose, polyethylene glycol or soluplus in a solvent; and

b) removing the solvent to obtain amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier.

Yet in another aspect, the present invention provides pharmaceutical compositions comprising a therapeutically effective amount of amorphous solid dispersion of saxagliptin hydrochloride along with a pharmaceutically acceptable carrier, and at least one pharmaceutically acceptable excipient.

Brief Description of the Drawing

Figure 1 is a powder X-ray diffractogram patterns of amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier.

Powder X-ray diffraction spectrum was measured on a bruker AXS D8 advance powder X-ray diffractometer having a copper-Kα radiation. Approximately 500 mg of sample was gently flattered on a sample holder and scanned from 2 to 50 degrees two-theta, at 0.020 degrees two theta per step and a step time of 1 second. The sample was simply placed on the sample holder. The sample was rotated at 30 rpm at a voltage 40 kV and current 35 mA.

Detailed Description of the Invention

The term "room temperature" refers to temperature at about 25 to 35^{0}C.

According to one aspect of the present invention, there is provided amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier.

The powdered x-ray diffractogram (PXRD) of amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier is shown in figure 1.

Amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier having enhanced stability, dissolution properties that can be easily formulated into pharmaceutical compositions.

Preferably the pharmaceutically acceptable carriers may be one or more of copovidone, ethyl cellulose, hydroxypropyl methylcellulose, polyethylene glycol or soluplus. The said pharmaceutically acceptable carriers are used to facilitate the presence of an amorphous saxagliptin hydrochloride.

The term "solid dispersion" herein refers to a composition prepared by dissolving or dispersing a substituted saxagliptin hydrochloride in an organic solvent or mixture of organic solvents with one or more pharmaceutically acceptable carriers and converting the solution or dispersion to a solid form.

According to another aspect of the present invention, there is provided a process for the preparation of amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier, which comprises:

a) preparing a solution comprising a mixture of saxagliptin hydrochloride and one or more pharmaceutically acceptable carriers selected from copovidone, ethyl cellulose, hydroxypropyl methylcellulose, polyethylene glycol or soluplus in a solvent; and

b) removing the solvent to obtain amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier.

Saxagliptin hydrochloride used in step (a) may preferably be saxagliptin hydrochloride obtained by the known process.

The solvent used in step (a) may preferably be a solvent or a mixture of solvents selected from dimethyl sulfoxide, dimethylacetamide, dimethylformamide, methanol, ethanol, isopropanol, n-butanol and n-pentanol, and more preferably the solvents are dimethyl sulfoxide, dimethylacetamide, dimethylformamide and methanol.

Preferably the pharmaceutically acceptable carriers used in step (a) may be selected from copovidone, soluplus or hydroxypropyl methylcellulose.

The solvent may be removed from the solution in step (b) by known methods, for example, distillation or spray drying.

The distillation of the solvent may be carried out at atmospheric pressure or at reduced pressure. The distillation may preferably be carried out until the solvent is almost completely distilled off.

As used herein, "reduced pressure" refers to a pressure of less than 100 mmHg.

The term “spray drying” refers to is a method of producing a dry powder from a liquid or slurry by rapidly drying with a hot gas.

According to another aspect of the present invention, there is provided pharmaceutical compositions comprising a therapeutically effective amount of amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier and along with pharmaceutically acceptable excipients, and at least one pharmaceutically acceptable excipient. The amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier may preferably be formulated into tablets, capsules, suspensions, dispersions, injectables or other pharmaceutical forms.

Preferably the present invention provides a pharmaceutical composition containing said solid dispersion along with the pharmaceutically acceptable excipients such as diluents, chelating agents, disintegrant, glidant, binders, surfactants, coloring agents and/or luricants.

Specific examples of binders include methyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, polyvinylpyrrolidone, gelatin, gum Arabic, ethyl cellulose, polyvinyl alcohol, pullulan, pregelatinized starch, agar, tragacanth, sodium alginate, propylene glycol, and the like.

Specific examples of diluents include calcium carbonate, calcium phosphate-dibasic, calcium phosphate-tribasic, calcium sulfate, microcrystalline cellulose, cellulose powdered, dextrates, dextrins, dextrose excipients, fructose, kaolin, lactitol, lactose, mannitol, sorbitol, starch, starch pregelatinized, sucrose, sugar compressible, sugar confectioners, and the like and mixtures thereof.

Surfactants include both non-ionic and ionic (cationic, anionic and zwitterionic) surfactants suitable for use in pharmaceutical dosage forms. These include polyethoxylated fatty acids and its derivatives, for example, polyethylene glycol 400 distearate, polyethylene glycol-20 dioleate, polyethylene glycol 4 – 150 mono dilaurate, and polyethylene glycol – 20 glyceryl stearate; alcohol – oil transesterification products, for example, polyethylene glycol – 6 corn oil; polyglycerized fatty acids, for example, polyglyceryl – 6 pentaoleate; propylene glycol fatty acid esters, for example, propylene glycol monocaprylate; mono and diglycerides, for example, glyceryl ricinoleate; sterol and sterol derivatives; sorbitan fatty acid esters and its derivatives, for example, polyethylene glycol – 20 sorbitan monooleate and sorbitan monolaurate; polyethylene glycol alkyl ether or phenols, for example, polyethylene glycol – 20 cetyl ether and polyethylene glycol – 10 – 100 nonyl phenol; sugar esters, for example, sucrose monopalmitate; polyoxyethylene – polyoxypropylene block copolymers known as "poloxamer"; ionic surfactants, for example, sodium caproate, sodium glycocholate, soy lecithin, sodium stearyl fumarate, propylene glycol alginate, octyl sulfosuccinate disodium, and palmitoyl carnitine; and the like and mixtures thereof.

Specific examples of disintegrants include low-substituted hydroxypropylcellulose (L-HPC), sodium starch glycollate, carboxymethyl cellulose, calcium carboxymethyl cellulose, sodium carboxymethyl cellulose, croscarmellose sodium A-type (Ac-di-sol), starch, crystalline cellulose, hydroxypropyl starch, pregelatinized starch, and the like and mixtures thereof.

Specific examples of lubricants/glidants include colloidal silicon dioxide, stearic acid, magnesium stearate, calcium stearate, talc, hydrogenated castor oil, sucrose esters of fatty acid, microcrystalline wax, yellow beeswax, white beeswax, and the like and mixtures thereof.

Coloring agents include any FDA approved colors for oral use.

The invention will now be further described by the following examples, which are illustrative rather than limiting.

Examples

Example 1:

Preparation of saxagliptin hydrochloride

Tert-butyl N-[(1S)-2-[(1S,3S,5S)-3-cyano-2-azabicylo[3.1.0]hexan-2yl]-1-[(3S,5R,7S)-3-hydroxyadamantan-1-yl]-2-oxoethyl]carbamate (100 gm) was dissolved in isopropyl alcohol (100 ml) and water (100 ml) and then added concentrated hydrochloric acid (35 ml) at room temperature. The contents were heated to 65^{0}C and stirred for 1 hour. Water (200 ml) was added to the solution at 65^{0}C and then cooled to room temperature. To the reaction mass was added methylene chloride (600 ml), sodium hydroxide (10N, 30 gm) and water (20 ml) at room temperature. The pH of the reaction mass was adjusted to 9.0 to 9.5 with potassium carbonate solution (24%) and then added water (20 ml) and sodium chloride (125 gm). The reaction mass was stirred for 45 minutes and then the layers were separated. The organic layer was dried with sodium sulfate and then concentrated to obtain a residual mass. To the residual mass was added ethyl acetate (170 ml) and then cooled to 10 to 15^{0}C. Water (170 ml) was added to the reaction mixture slowly and stirred for 3 hours at 10 to 15^{0}C. The separated solid was filtered and then dried at 30 to 35^{0}C for 5 hours to obtain a solid. The solid obtained was dissolved in methylene chloride (3000 ml) at room temperature. The solution was then cooled to 0 to 5^{0}C and then added hydrochloric acid (11%) in ethyl acetate (50 ml). The reaction mass was stirred for 3 hours at 0 to 5^{0}C and filtered. The solid obtained was dried to obtain 50 gm of saxagliptin hydrochloride.

Example 2:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with copovidone

A mixture of saxagliptin hydrochloride (50 gm) as obtained in example 1 and copovidone (50 gm) was dissolved in methanol (300 ml) at room temperature. The solution was filtered through hy-flow bed and the solvent was distilled off under reduced

pressure at below 50^0C and then dried to obtain 95 gm of amorphous saxagliptin hydrochloride solid dispersion with copovidone.

Example 3:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with copovidone

A mixture of saxagliptin hydrochloride (50 gm) and copovidone (100 gm) was dissolved in methanol (450 ml) at room temperature. The solution was filtered through hy-flow bed and the solvent was distilled off under reduced pressure at below 50^0C and then dried to obtain 142 gm of amorphous saxagliptin hydrochloride solid dispersion with copovidone.

Example 4:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with copovidone

A mixture of saxagliptin hydrochloride (50 gm) and copovidone (150 gm) was dissolved in methanol (600 ml) at room temperature. The solution was filtered through hy-flow bed and the solvent was distilled off under reduced pressure at below 50^0C and then dried to obtain 190 gm of amorphous saxagliptin hydrochloride solid dispersion with copovidone.

Example 5:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with copovidone

Example 2 was repeated using dimethylformamide solvent instead of methanol solvent to obtain amorphous saxagliptin hydrochloride solid dispersion with copovidone.

Example 6:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with copovidone

Example 2 was repeated using dimethylacetamide solvent instead of methanol solvent to obtain amorphous saxagliptin hydrochloride solid dispersion with copovidone.

Example 7:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with copovidone

Example 2 was repeated using dimethyl sulfoxide solvent instead of methanol solvent to obtain amorphous saxagliptin hydrochloride solid dispersion with copovidone.

Example 8:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with copovidone

Example 2 was repeated using ethanol solvent instead of methanol solvent to obtain amorphous saxagliptin hydrochloride solid dispersion with copovidone.

Example 9:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with hydroxypropyl methylcellulose

A mixture of saxagliptin hydrochloride (20 gm) and hydroxypropyl methylcellulose (20 gm) was dissolved in methanol (120 ml) at room temperature. The solution was filtered through hy-flow bed and the solvent was distilled off under reduced pressure at below 50^0C and then dried to obtain 37 gm of amorphous saxagliptin hydrochloride solid dispersion with hydroxypropyl methylcellulose.

Example 10:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with hydroxypropyl methylcellulose

Example 9 was repeated using dimethylformamide solvent instead of methanol solvent to obtain amorphous saxagliptin hydrochloride solid dispersion with hydroxypropyl methylcellulose.

Example 11:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with hydroxypropyl methylcellulose

Example 9 was repeated using dimethylacetamide solvent instead of methanol solvent to obtain amorphous saxagliptin hydrochloride solid dispersion with hydroxypropyl methylcellulose.

Example 12:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with hydroxypropyl methylcellulose

Example 9 was repeated using dimethyl sulfoxide solvent instead of methanol solvent to obtain amorphous saxagliptin hydrochloride solid dispersion with hydroxypropyl methylcellulose.

Example 13:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with hydroxypropyl methylcellulose

Example 9 was repeated using ethanol solvent instead of methanol solvent to obtain amorphous saxagliptin hydrochloride solid dispersion with hydroxypropyl methylcellulose.

Example 14:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with soluplus

A mixture of saxagliptin hydrochloride (10 gm) and soluplus (20 gm) was dissolved in methanol (150 ml) at room temperature. The solution was filtered through hy-flow bed and the solvent was distilled off under reduced pressure at below 50^0C and then dried to obtain 29 gm of amorphous saxagliptin hydrochloride solid dispersion with soluplus.

Example 15:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with soluplus

Example 14 was repeated using dimethylformamide solvent instead of methanol solvent to obtain amorphous saxagliptin hydrochloride solid dispersion with soluplus.

Example 16:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with soluplus

Example 14 was repeated using dimethylacetamide solvent instead of methanol solvent to obtain amorphous saxagliptin hydrochloride solid dispersion with soluplus.

Example 17:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with soluplus

Example 14 was repeated using dimethyl sulfoxide solvent instead of methanol solvent to obtain amorphous saxagliptin hydrochloride solid dispersion with soluplus.

Example 18:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with soluplus

Example 14 was repeated using ethanol solvent instead of methanol solvent to obtain amorphous saxagliptin hydrochloride solid dispersion with soluplus.

Example 19:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with polyethylene glycol

A mixture of saxagliptin hydrochloride (20 gm) and polyethylene glycol (30 gm) was dissolved in methanol (150 ml) at room temperature. The solution was filtered through hy-flow bed and the solvent was distilled off under reduced pressure at below 50^0C to obtain 46 gm of amorphous saxagliptin hydrochloride solid dispersion with polyethylene glycol.

Example 20:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with ethyl cellulose

A mixture of saxagliptin hydrochloride (10 gm) and ethyl cellulose (10 gm) was dissolved in methanol (80 ml) at room temperature. The solution was filtered through hy-flow bed and the solvent was distilled off under reduced pressure at below 50^0C to obtain 18 gm of amorphous saxagliptin hydrochloride solid dispersion with ethyl cellulose.

Example 21:

Preparation of amorphous saxagliptin hydrochloride solid dispersion with copovidone

Tert-butyl N-[(1S)-2-[(1S,3S,5S)-3-cyano-2-azabicylo[3.1.0]hexan-2yl]-1-[(3S,5R,7S)-3-hydroxyadamantan-1-yl]-2-oxoethyl]carbamate (100 gm) was dissolved in isopropyl alcohol (100 ml) and water (100 ml) and then added concentrated hydrochloric acid (35 ml) at room temperature. The contents were heated to 65^0C and stirred for 1 hour. Water (200 ml) was added to the solution at 65^0C and then cooled to room temperature. To the reaction mass was added methylene chloride (600 ml), sodium hydroxide (10N, 30 gm) and water (20 ml) at room temperature. The pH of the reaction mass was adjusted to 9.0 to 9.5 with potassium carbonate solution (24%) and then added water (20 ml) and sodium chloride (125 gm). The reaction mass was stirred for 45 minutes and then the layers were separated. The organic layer was dried with sodium sulfate and then concentrated to obtain a residual mass. To the residual mass was added ethyl acetate (170 ml) and then cooled to 10 to 15^0C. Water (170 ml) was added to the reaction mixture slowly and stirred for 3 hours at 10 to 15^0C. The separated solid was filtered and then dried at 30 to 35^0C for 5 hours to obtain a solid. The solid obtained was dissolved in methylene chloride (3000 ml) at room temperature. The solution was then cooled to 0 to 5^0C and then added hydrochloric acid (11%) in ethyl acetate (50 ml). The reaction mass was stirred for 3 hours at 0 to 5^0C and then added copovidone (50 gm) and methanol (300 ml) at room temperature. The solution was filtered through hy-flow bed and the solvent was distilled off under reduced pressure at below 50^0C. The solid obtained was dried to obtain 95 gm of amorphous saxagliptin hydrochloride solid dispersion with copovidone.

Example 22:

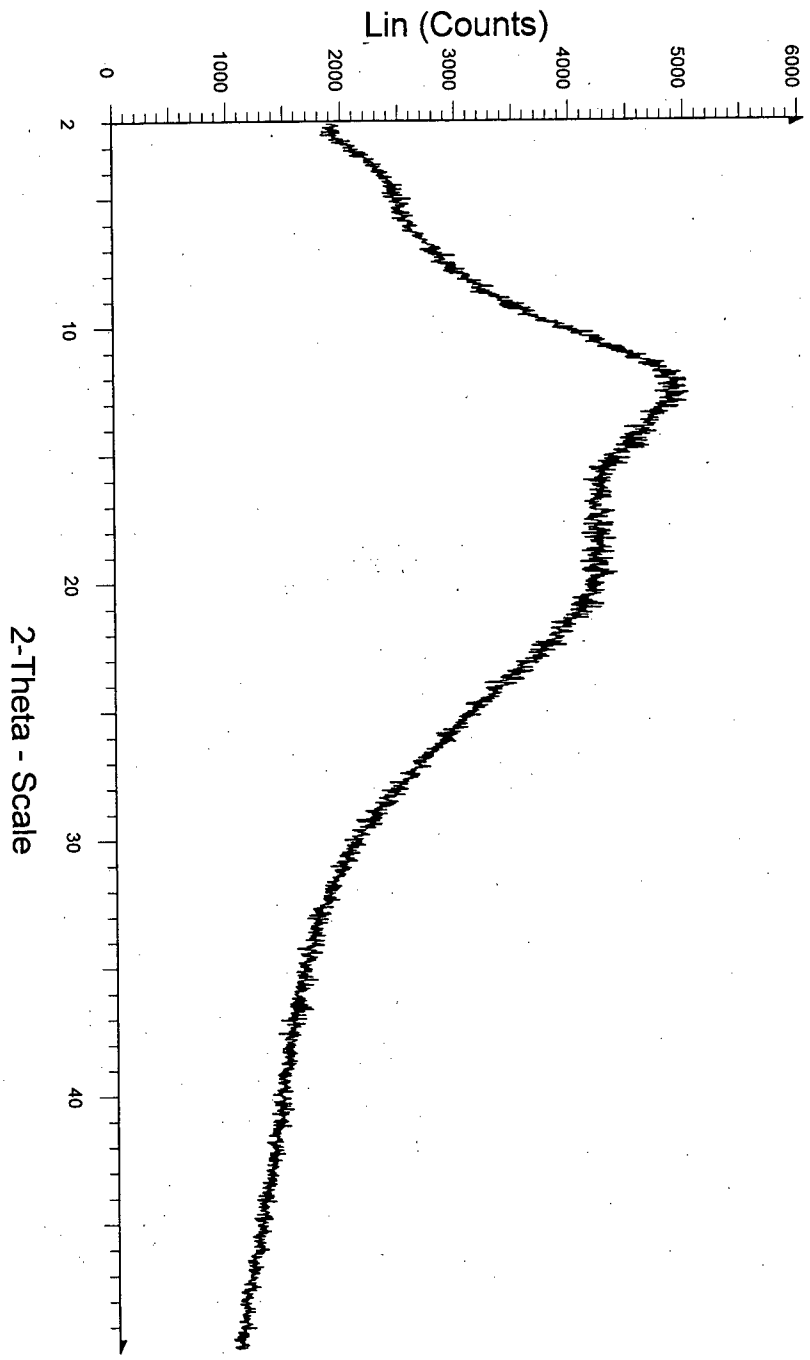
Preparation of amorphous saxagliptin hydrochloride solid dispersion with hydroxypropyl methylcellulose

Tert-butyl N-[(1S)-2-[(1S,3S,5S)-3-cyano-2-azabicylo[3.1.0]hexan-2yl]-1-[(3S,5R,7S)-3-hydroxyadamantan-1-yl]-2-oxoethyl]carbamate (100 gm) was dissolved in isopropyl alcohol (100 ml) and water (100 ml) and then added concentrated hydrochloric acid (35 ml) at room temperature. The contents were heated to 65^{0}C and stirred for 1 hour. Water (200 ml) was added to the solution at 65^{0}C and then cooled to room temperature. To the reaction mass was added methylene chloride (600 ml), sodium hydroxide (10N, 30 gm) and water (20 ml) at room temperature. The pH of the reaction mass was adjusted to 9.0 to 9.5 with potassium carbonate solution (24%) and then added water (20 ml) and sodium chloride (125 gm). The reaction mass was stirred for 45 minutes and then the layers were separated. The organic layer was dried with sodium sulfate and then concentrated to obtain a residual mass. To the residual mass was added ethyl acetate (170 ml) and then cooled to 10 to 15^{0}C. Water (170 ml) was added to the reaction mixture slowly and stirred for 3 hours at 10 to 15^{0}C. The separated solid was filtered and then dried at 30 to 35^{0}C for 5 hours to obtain a solid. The solid obtained was dissolved in methylene chloride (3000 ml) at room temperature. The solution was then cooled to 0 to 5^{0}C and then added hydrochloric acid (11%) in ethyl acetate (50 ml). The reaction mass was stirred for 3 hours at 0 to 5^{0}C and then added hydroxypropyl methylcellulose (50 gm) and methanol (300 ml) at room temperature. The solution was filtered through hy-flow bed and the solvent was distilled off under reduced pressure at below 50^{0}C. The solid obtained was dried to obtain 92 gm of amorphous saxagliptin hydrochloride solid dispersion with copovidone.

We claim:

1. Amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier.
2. The amorphous solid dispersion of claim 1, wherein the pharmaceutically acceptable carriers may be one or more of copovidone, ethyl cellulose, hydroxypropyl methylcellulose, polyethylene glycol or soluplus.
3. The amorphous solid dispersion of claim 1, having a powder X-ray diffractogram as shown in figure 1.
4. A process for the preparation of amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier, which comprises:
   a. preparing a solution comprising a mixture of saxagliptin hydrochloride and one or more pharmaceutically acceptable carriers selected from copovidone, ethyl cellulose, hydroxypropyl methylcellulose, polyethylene glycol or soluplus in a solvent; and
   b. removing the solvent to obtain amorphous solid dispersion of saxagliptin hydrochloride in combination with a pharmaceutically acceptable carrier.
5. The process as claimed in claim 4, wherein the solvent used in step (a) is a solvent or a mixture of solvents selected from dimethyl sulfoxide, dimethylacetamide, dimethylformamide, methanol, ethanol, isopropanol, n-butanol and n-pentanol.
6. The process as claimed in claim 5, wherein the solvents are dimethyl sulfoxide, dimethylacetamide, dimethylformamide and methanol.
7. The process as claimed in claim 4, wherein the pharmaceutically acceptable carriers used in step (a) is selected from copovidone, soluplus or hydroxypropyl methylcellulose.
8. Pharmaceutical compositions comprising a therapeutically effective amount of amorphous solid dispersion of saxagliptin hydrochloride along with pharmaceutically acceptable excipients, and at least one pharmaceutically acceptable excipient.
9. The pharmaceutical composition as claimed in claim 8, wherein the amorphous solid dispersion of saxagliptin hydrochloride is formulated into tablets, capsules, suspensions, dispersions or injectables.

Fig. 1/1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