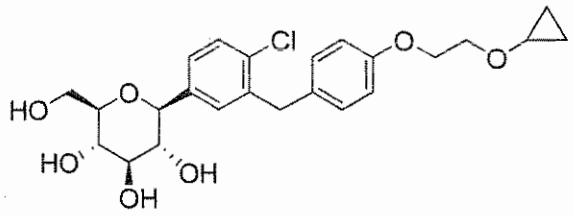
[0009] The compound of the present invention has been prepared according to the methods of U.S. Publication No. 2009/0118201, filed August 22, 2008, U.S. Application No. 12/545,400, and PCT/US2009/054585, now WO2010/022313, both filed August 21, 2009. The aim of the present invention is to provide a stable crystalline form of the compound which meets important requirements imposed on pharmaceutically active substances as mentioned above.

BRIEF SUMMARY ~~OF THE INVENTION~~

[0010] The present disclosure~~invention~~ provides crystalline forms of (2S,3R,4R,5S,6R)-2-(4-chloro-3-(4-(2-cyclopropoxyethoxy)benzyl)phenyl)-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol having an inhibitory effect on sodium-dependent glucose cotransporter 2 (SGLT2). The present disclosure~~invention~~ also provides pharmaceutical compositions, methods of preparing the crystalline form of the compound, and methods of using the compound, independently or in combination with other therapeutic agents, for treating diseases and conditions which are affected by SGLT2 inhibition.

[0010a] In a first aspect of the present disclosure, there is provided a crystalline form of the compound of the formula:



characterized by an X-ray powder diffraction (XRPD) pattern that comprises peaks at 11.2, 12.9, 15.5, 17.8, 19.1, 20.0 and 20.7 degrees 2θ (± 0.1 degrees 2θ), wherein said XRPD is made using $CuK_{\alpha 1}$ radiation.

[0010b] In a second aspect of the present disclosure, there is provided a pharmaceutical composition comprising a pharmaceutically acceptable excipient and a crystalline form of the compound (2S,3R,4R,5S,6R)-2-(4-chloro-3-(4-(2-cyclopropoxyethoxy)benzyl)phenyl)-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol as defined above.

[0010c] In a third aspect of the present disclosure, there is provided a method for making a crystalline form of the compound as defined above, said method comprising the steps: (a) combining (2S,3R,4R,5S,6R)-2-(4-chloro-3-(4-(2-cyclopropoxyethoxy)benzyl)phenyl)-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol bis(L-proline) complex and a suitable solvent with mixing to form a solution; (b) adding a precipitating solvent to said solution to provide a mixture; and (c) isolating said crystalline form from said mixture.

[0010d] In a fourth aspect of the present disclosure, there is provided a method for making a crystalline form of the compound as defined above, said method comprising the steps: (a) combining (2S,3R,4R,5S,6R)-2-(4-chloro-3-(4-(2-cyclopropoxyethoxy)benzyl)phenyl)-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol and a suitable solvent with mixing to form a solution; and (b) isolating said crystalline form from said solution.

[0010e] In a fifth aspect of the present disclosure, there is provided the use of a composition comprising a crystalline form of the compound as defined above in the manufacture of a medicament for treating a disease or condition selected from the group consisting of type 1 diabetes mellitus, type 2 diabetes mellitus, hyperglycemia, diabetic complications, insulin resistance, metabolic syndrome, hyperinsulinemia, hypertension, hyperuricemia, obesity, edema, dyslipidemia, chronic heart failure, atherosclerosis, and cancer.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] **Figure 1** provides the X-ray powder diffraction (XRPD) spectra of crystalline (2S,3R,4R,5S,6R)-2-(4-chloro-3-(4-(2-cyclopropoxyethoxy)benzyl)phenyl)-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol.

[0012] **Figure 2** provides a Table of XRPD data for the XRPD spectra in **Figure 1**.

[0013] **Figure 3** provides the Raman spectra of crystalline (2S,3R,4R,5S,6R)-2-(4-chloro-3-(4-(2-cyclopropoxyethoxy)benzyl)phenyl)-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol.

[0014] **Figure 4** provides a Raman peak list for the Raman spectra in **Figure 3**.

[0015] **Figure 5** provides the thermal gravimetric analysis (TGA) of crystalline (2S,3R,4R,5S,6R)-2-(4-chloro-3-(4-(2-cyclopropoxyethoxy)benzyl)phenyl)-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol.

a *c* of 16.560 Å,

an α of 90°,

a β of 95.71°,

a γ of 90°,

a volume of 1162.1 $Å^3$/cell,

a V/Z of 581.1 $Å^3$/asymmetric unit,

an assumed composition of $C_{24}H_{29}O_7Cl$, and

a density of 1.329 g/cm^3.

13. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a crystalline form of the compound (2S,3R,4R,5S,6R)-2-(4-chloro-3-(4-(2-cyclopropoxyethoxy)benzyl)phenyl)-6-(hydroxymethyl)tetrahydro-2*H*-pyran-3,4,5-triol of claim 1.