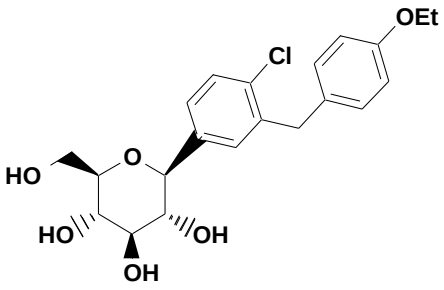
Claims

1. A crystalline structure of a compound of formula I



I

selected from the group consisting of the mono ethanol dihydrate (EtOH; form SA-1), mono ethylene glycol dihydrate (EG) structure (form SB-1) and mono ethylene glycol dihydrate (EG) structure (form SB-2).

2. The crystalline structure as defined in Claim 1 wherein each of said structures is in substantially pure form.

3. (A) The crystalline structures as defined in Claim 1 selected from the group consisting of mono ethanol dihydrate (EtOH; form SA-1) characterized by one or more of the unit cell parameters substantially equal to the following:

Cell dimensions:

a= 11.519(1) Å

b = 4.799(1) Å

c = 22.648(1) Å

α = - degrees

β = 94.58(1) degrees

γ = - degrees

Space group = P21

Molecules/asymmetric unit 1

wherein measurement of said crystalline structure is at -50°C and which is characterized by fractional atomic coordinates substantially as listed in Table 6;

(B) the crystalline mono ethylene glycol dihydrate structure (EG; form SB-1) characterized by one or more unit cell parameters substantially equal to the following: a solid state ^{13}C NMR spectrum having substantially similar peak positions at 12.49, 59.16, 60.61, 60.69, 68.10, 72.51, 76.11, 78.51, 79.02, 112.09, 125.16, 126.47, 127.38, 128.61, 129.02, 129.73, 135.62, 137.48, and 154.70 ppm, as determined on a 400MHz spectrometer relative to TMS at zero:

Cell dimensions:

a = 11.593(8) Å

b = 4.766(5) A

c = 22.78(3) Å

α = - degrees

β = 93.38(9) degrees

γ = - degrees

Space group P21

Molecules/asymmetric unit 1

wherein measurement of said crystalline structure is at -50°C and which is characterized by fractional atomic coordinates substantially as listed in Table 8;

(C) the crystalline mono ethylene glycol dihydrate structure (EG; SB-2) characterized by one or more unit cell parameters substantially equal to the following:

Cell dimensions:

a = 11.4950(1) Å

b = 4.7443(1) Å

c = 44.4154(5) A

α = - degrees

β = - degrees

γ = - degrees

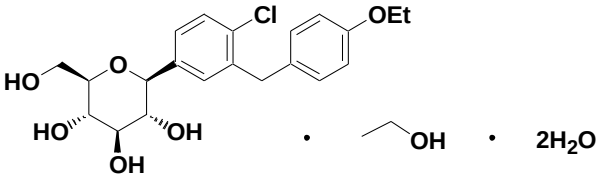
Space group P21 21 21

Molecules/asymmetric unit 1

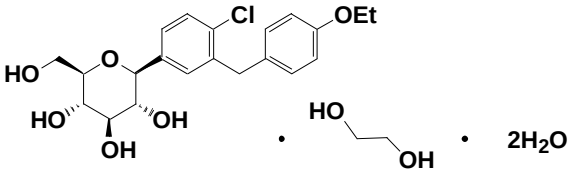
wherein measurement of said crystalline structure is at room temperature and which is characterized by fractional atomic coordinates substantially as listed in Table 10.

4. A pharmaceutical composition comprising an effective amount of a crystal structure of a compound of formula I as defined in any one of Claims 1 to 3 and a pharmaceutically acceptable carrier or diluent.

5. The pharmaceutical composition as defined in Claim 4 wherein said crystal structure is selected from the group consisting of:

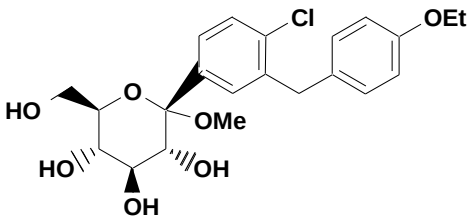


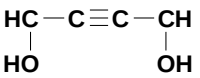
Ic;



Id or Ie
(SB-1 or SB-2)

6. The crystalline structure of the 1,4-butyne-diol solvate of formula If



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If

characterized by one or more unit cell parameters substantially equal to the following:

Cell dimensions:

a = 21.576(7) Å

b = 6.755(1) Å

c = 18.335(5) Å

α = - degrees

β = 102.96(1) degrees

γ = - degrees

Space group C2

Molecules/asymmetric unit 1

wherein measurement of said crystalline structure is at 25°C and which is characterized by fractional atomic coordinates substantially as listed in Table 12, or

Cell dimensions:

a = 21.537(4) Å

b = 6.7273(6) A

c = 18.267(3) Å

α = - degrees

β = 102.924(7) degrees

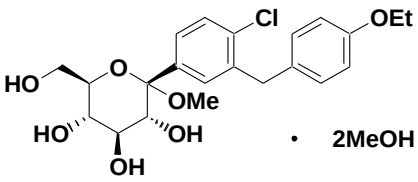
γ = - degrees

Space group C2

Molecules/asymmetric unit 1

wherein measurement of said crystalline structure is at -50°C, or proton NMR having substantially similar peak positions as listed in Table 2A.

7. A crystal structure of a compound of the dimethanol solvate structure Ig



Ig

characterized by one or more unit cell parameters substantially equal to the following:

Cell dimensions:

a = 20.948(3) Å

b = 6.794(2) Å

c =

α = - degrees

β =102.91 (2) degrees

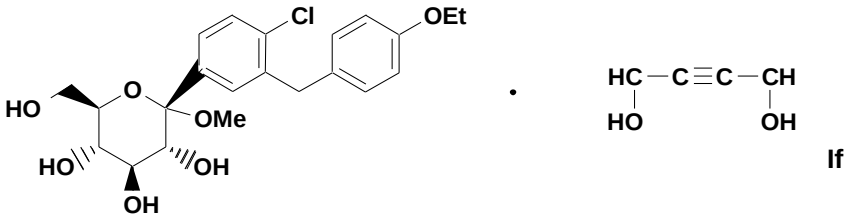
γ = - degrees

Space group C2

Molecules/asymmetric unit 1

wherein measurement of said crystalline structure is at -50°C and which is characterized by fractional atomic coordinates substantially as listed in Table 14, or proton NMR having substantially similar peak positions as listed in Table 2B.

8. A process for preparing the crystalline 1,4-butyne-diol solvate compound If

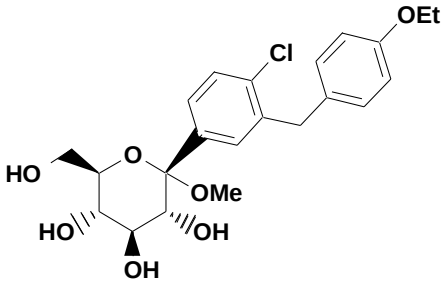


If

as defined in Claim 6

which comprises

a) mixing compound B of the structure



B

with toluene and ethyl acetate;

b) heating the mixture at a temperature within the range from about 50 to about 70°C;

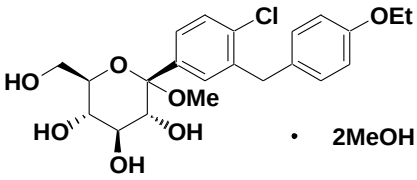
c) adding 1,4-butyne-diol;

d) heating the mixture until the diol dissolves;

e) adding seeds of compound If to the solution; and

f) cooling the mixture to form crystals of compound If.

9. A process for preparing the dimethanol solvate Ig

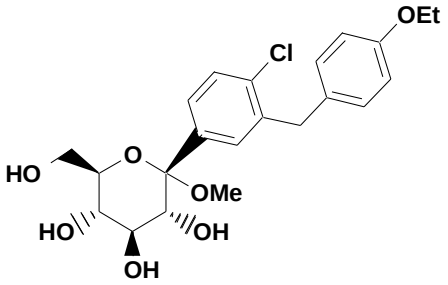


Ig

as defined in Claim 7

which comprises

a) treating compound B of the structure



B

with

methanol,

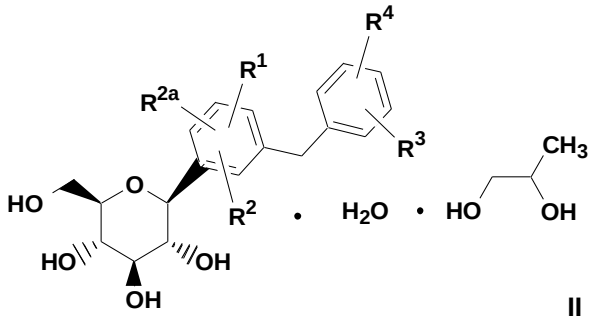
a mixture of methanol and toluene, or

a mixture of methanol, toluene and heptane, or a mixture of methanol, MTBE and heptane, to form a solution;

b) optional adding seeds of the formula Ig dimethanol solvate to the solution; and

c) forming crystals of the dimethanol solvate Ig.

10. A crystalline structure of a compound of formula II



II

which is the (S)-propylene glycol solvate or the (R)-propylene glycol solvate or a mixture thereof,

wherein

R^1, R^2 and R^{2a} are independently hydrogen, OH, OR^5, alkyl, $-OCHF_2$, $-OCF_3$, $-SR^{5a}$ or halogen;

R^3 and R^4 are independently hydrogen, OH, OR^{5b}, alkyl, alkene, alkyne, cycloalkyl, CF_3, $-OCHF_2$, $-OCF_3$, halogen, $-CONR^6R^{6a}$, $-CO_2R^{5c}$, $-CO_2H$, $-COR^{6b}$, $-CH(OH)R^{6c}$, $-CH(OR^{5d})R^{6d}$, -CN, $-NHCOR^{5e}$, $-NHSO_2R^{5f}$, $-NHSO_2$Aryl, $-SR^{5g}$, $-SOR^{5h}$, $-SO_2R^{5i}$, $-SO_2$Aryl, or a five, six or seven membered heterocycle which may contain 1 or 4 heteroatoms in the ring which are N, O, S, SO, and/or SO_2, or R^3 and R^4 together with the carbons to which they are attached form an annelated five, six or seven membered carbocycle or heterocycle which may contain 1 to 4 heteroatoms in the ring which are N, O, S, SO, and/or SO_2;

R^5, R^{5a}, R^{5b}, R^{5c}, R^{5d}, R^{5e}, R^{5f}, R^{5g}, R^{5h} and R^{5i} are independently alkyl, alkene or alkyne; and

R^6, R^{6a}, R^{6b}, R^{6c} and R^{5d} are independently hydrogen, alkyl, aryl, alkylaryl or cycloalkyl, or R^6 and R^{6a} together with the nitrogen to which they are attached form an annelated five, six or seven membered heterocycle which may contain 1 to 4 heteroatoms in the ring which are N, O, S, SO, and/or SO_2.

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