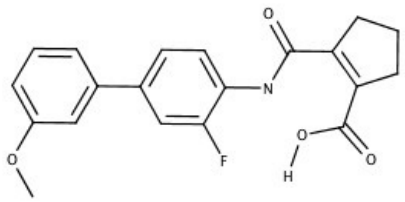
Claims

1. A crystalline polymorph A of the hydrate of the Ca salt of a compound according to formula I



formula I

with a molar ratio of said compound according to formula I to calcium 2±0.3,

which is characterized by:

an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2theta at ±0.2 of the values 2theta = 5.91°, 9.64°, 16.78°, 17.81°, 19.81°, 25.41°.

2. A crystalline polymorph A of the hydrate of the Ca salt of a compound according to formula I according to claim 1, which is white.

3. A crystalline polymorph A of the hydrate of the Ca salt of a compound according to formula I according to claim 1 or 2, wherein the characteristic peaks which have degree 2theta at ±0.2 of the values shown below:

Table 1: Peak-list of polymorph A of Ca salt of vidofludimus

Angle 2theta °	d value Angstrom	Intensity
5.91	14.95	vs
6.83	12.93	vw
9.64	9.17	w
11.33	7.80	w
11.82	7.48	w
12.98	6.81	vw
13.70	6.46	vw
14.27	6.20	vw
15.04	5.89	w
15.44	5.73	vw
16.78	5.28	s
17.81	4.98	m
18.25	4.86	w
18.58	4.77	vw

19.39	4.57	w
19.81	4.48	w
20.53	4.32	vw
21.26	4.18	vw
22.63	3.93	vw
23.16	3.84	vw
23.96	3.71	w
24.73	3.60	vw
25.41	3.50	s
26.12	3.41	w
26.44	3.37	w
27.25	3.27	w
27.55	3.24	w
28.45	3.13	w
28.91	3.09	vw
29.29	3.05	w
29.89	2.99	w
30.77	2.90	w
31.22	2.86	vw
31.60	2.83	w
32.13	2.78	w
33.25	2.69	vw
33.98	2.64	w
34.48	2.60	w
35.12	2.55	vw

as shown in Figure 1.

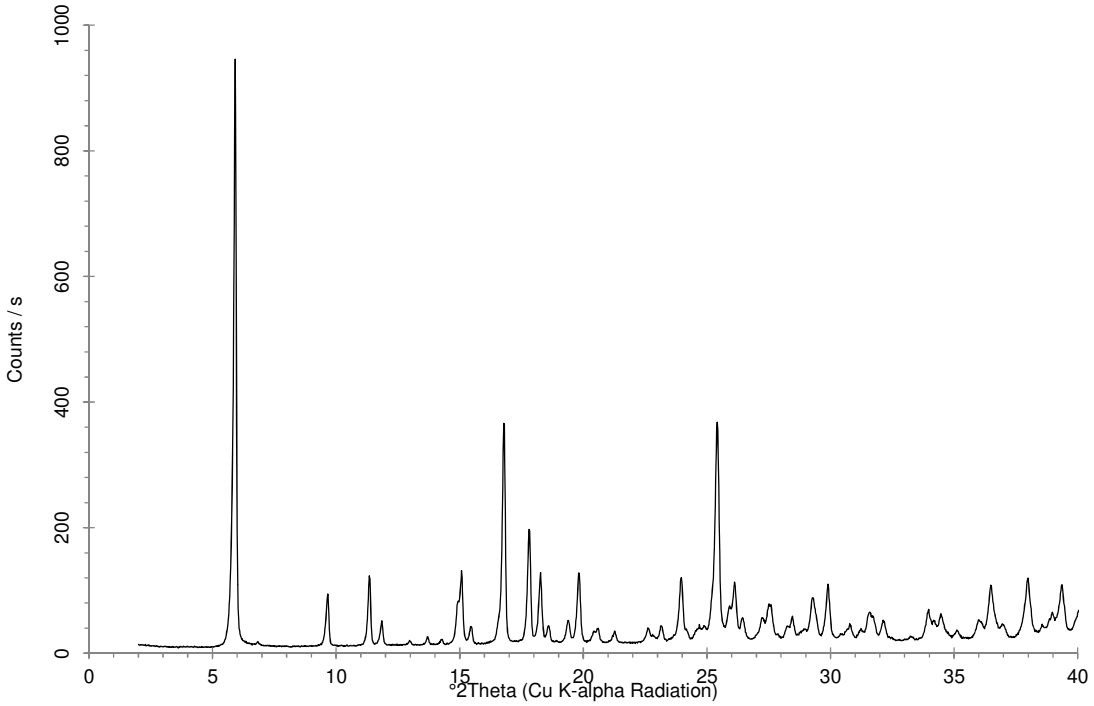


Figure 1: PXRD of polymorph A of the hydrate of the Ca salt of a compound according to formula I

4. A crystalline polymorph A of the hydrate of the Ca salt of a compound according to formula I according to any of claims 1 to 3 which is characterized by an FT Raman absorption spectrum having the following characteristic peaks expressed in cm^{-1} 1664, 1624, 1617, 1532, 1449, 1338 as shown in Figure 2.

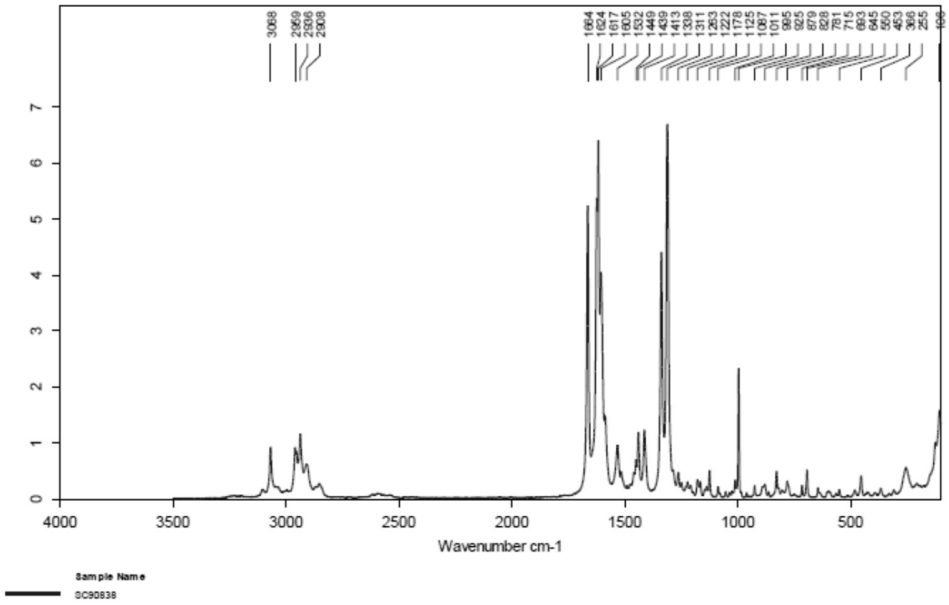


Figure 2: Raman spectrum of polymorph A of the hydrate of the Ca salt of a compound according to formula I

5. A crystalline polymorph A of the hydrate of the Ca salt of a compound according to formula I according to any of claims 1 to 4 which is characterized by an IR absorption spectrum having characteristic peaks expressed in cm^{-1} 1980, 1659, 1584, 1335, 1145, as shown in Figures 3a and 3b.

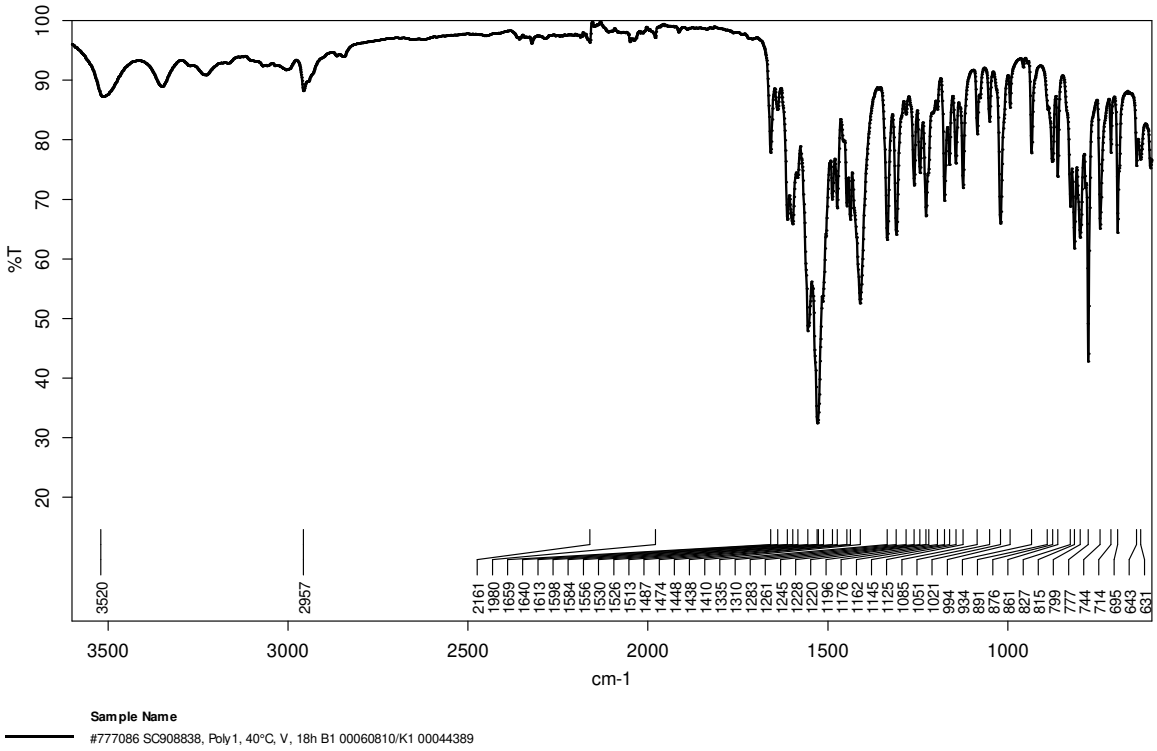


Figure 3a: IR spectrum of polymorph A of the hydrate of the Ca salt of a compound according to formula I, complete region

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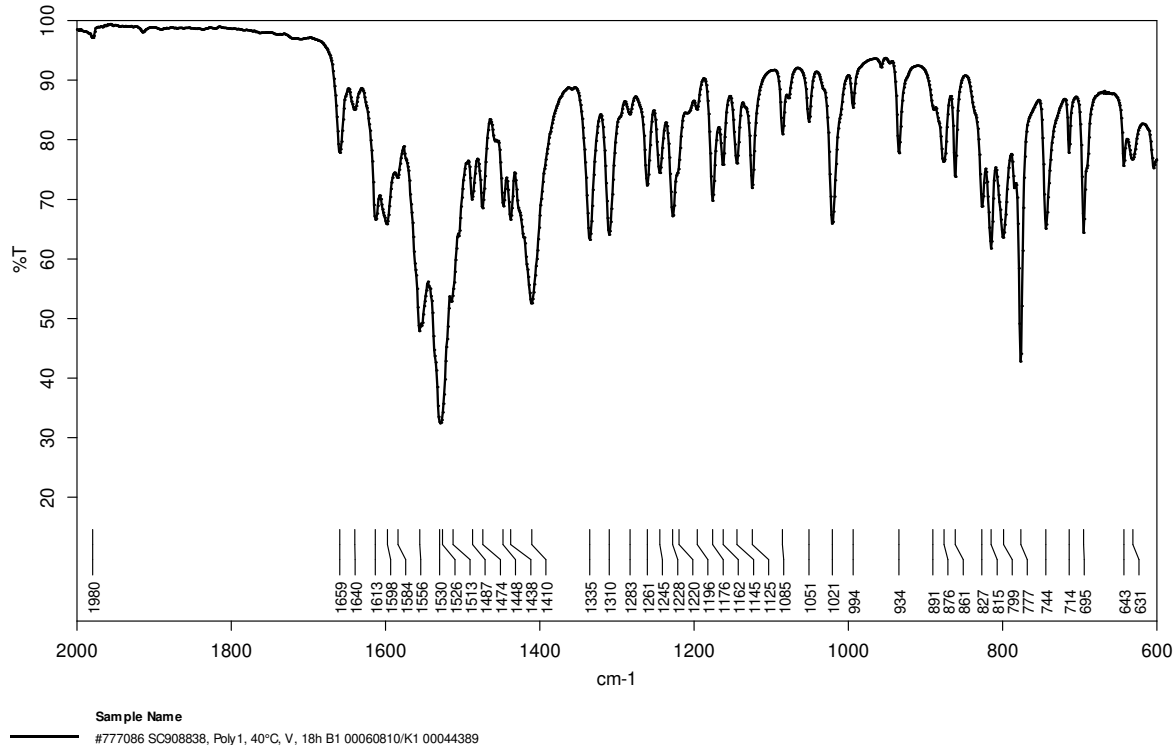

Figure 3b: IR spectrum of polymorph A of the hydrate of the Ca salt of a compound according to formula I, fingerprint region.

6. A crystalline polymorph A of the hydrate of the Ca salt of a compound according to formula I according to any of claims 1 to 5 which is characterized by an ^{1}H-NMR spectrum in DMSO having characteristic peaks expressed in ppm, 15.2, 8.3, 7.6, 7.5, 7.4, 7.2, 6.8, 3.8, 2.7, 1.6, as shown in Figure 4.

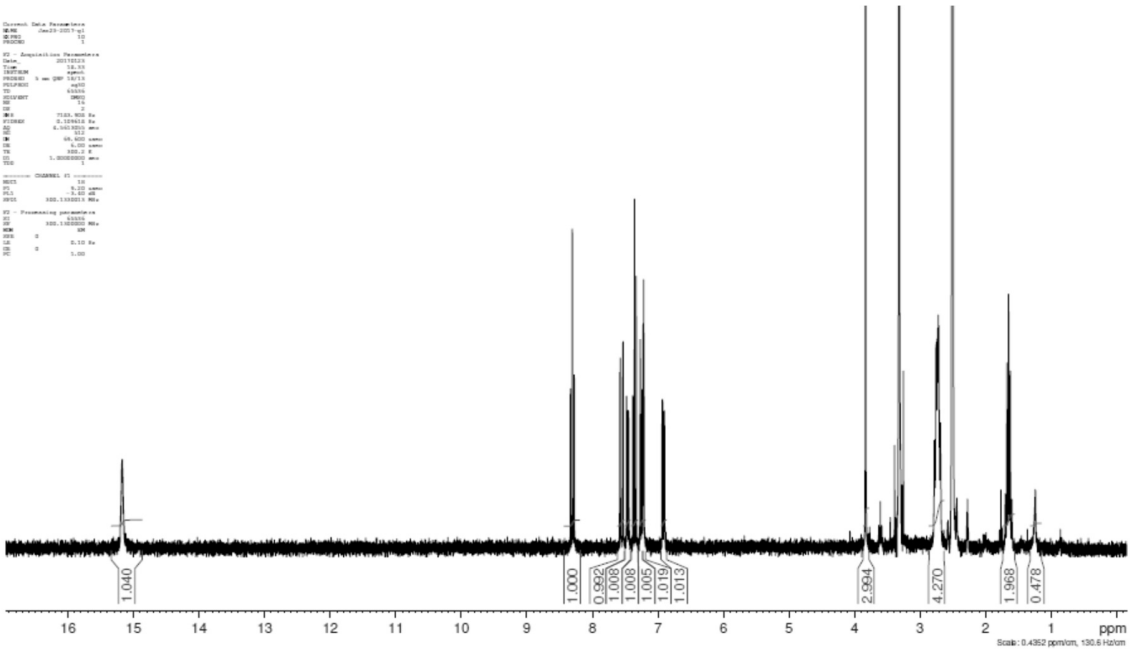

Figure 4: ^{1}H-NMR spectrum of polymorph A of the hydrate of the Ca salt of a compound according to formula I

7. A crystalline polymorph A of the hydrate of the Ca salt of a compound according to formula I according to any of claims 1 to 6, wherein the molar ratio of a compound according to formula I to water is about 1:1.

8. A pharmaceutical formulation comprising a crystalline polymorph A of the hydrate of the Ca salt of a compound according to formula I as defined in any of claims 1 to 7.

9. A pharmaceutical formulation according to claim 8, wherein the crystalline polymorph A of the hydrate of the Ca salt of a compound of formula I has a THF content of less than 720 ppm.

10. A crystalline polymorph A of the hydrate of the Ca salt of a compound according to formula I according to any of claims 1 to 6 or a pharmaceutical formulation according to claim 8 or 9 for use as a medicament.

11. A crystalline polymorph A of the hydrate of the Ca salt of a compound according to formula

I according to any of claims 1 to 7 or a pharmaceutical formulation according to claim 8 or 9 for use as in the treatment of a disease or a therapeutic indication selected from the group comprising rheumatism, acute immunological disorders, autoimmune diseases, diseases caused by malignant cell proliferation, inflammatory diseases, diseases that are caused by protozoal infestations in humans and animals, diseases that are caused by viral infections and Pneumocystis carinii, fibrosis, uveitis, rhinitis, asthma, athropathy,

graft versus host and host versus graft reactions, rheumatoid arthritis, multiple sclerosis, amyotrophic lateral sclerosis, lupus erythematosus, inflammatory bowel disease, and psoriasis.

12. A process for the manufacture of a crystalline polymorph A of the hydrate of the Ca salt of a compound according to formula I as defined in any of claims 1 to 7, wherein the process comprises the steps of

- providing a compound of formula I, also called Ca vidofludimus or a solvate and/or a hydrate thereof, preferably a crystalline polymorph of the Ca salt of vidofludimus or a solvate and/or a hydrate thereof,
- washing the Ca salt of vidofludimus or a solvate and/or a hydrate thereof with an aprotic organic solvent preferably selected from the group comprising DMF, DMSO, NMP, THF, acetone, dioxane, 2-methyl-THF or Methanol/CH_2Cl_2 (1:3), preferably acetone, and
- slurring the isolated Ca vidofludimus or a solvate and/or a hydrate thereof obtained in an alcoholic solvent and adding water to the slurry.

13. A process for the manufacture of a crystalline polymorph A of the hydrate of the Ca salt of a compound according to formula I as defined in any of claims 1 to 7 according to claim 12, wherein the process comprises the steps of

a) adding to a mixture of calcium hydroxide and free acid of a compound according to formula I or a solvate and/or a hydrate thereof an organic solvent and water

b) stirring the suspension obtained in step a) until a solution is obtained, wherein the suspension is preferably heated to 25 – 30 °C.

c) at least partially evaporating said organic solvent and water to obtain a suspension of the calcium salt of a compound according to formula I or a solvate and/or a hydrate thereof

d) adding an aprotic organic solvent, fully mixable with water to said suspension of the calcium salt of a compound according to formula I or a solvate and/or a hydrate thereof obtained in step c)

e) stirring the suspension obtained in step d), wherein the suspension is preferably heated to 15 – 25 °C.

f) recovering the calcium salt of a compound according to formula I or a solvate and/or a hydrate thereof from the mixture obtained in step e), and

g) washing the calcium salt of a compound according to formula I or a solvate and/or a hydrate thereof obtained in step f) with the aprotic organic solvent mentioned in step d).

h) slurring the isolated calcium salt a compound according to formula I or a solvate and/or a hydrate thereof obtained in step g) in an alcoholic solvent at 15 – 80°C.

i) adding water to the slurry obtained in step h) at 15 – 85°C

j) recovering the crystalline polymorph A of the hydrate of the calcium salt of a compound according to formula I from the mixture obtained in step i), and

k) washing the crystalline polymorph A of the hydrate of the calcium salt of a compound according to formula I obtained in step j) with the aprotic organic solvent mentioned in step d).

14. A process for the manufacture of a crystalline polymorph according to claim 13 wherein after step g) and step k) a drying step is added, and optionally subsequently a milling step and optionally subsequently a recrystallization step is added.

15. A process for the manufacture of a crystalline polymorph according to claim 13 or 14 wherein after step b) and before step c) the solution is filtered and then the filter is washed with said organic solvent.