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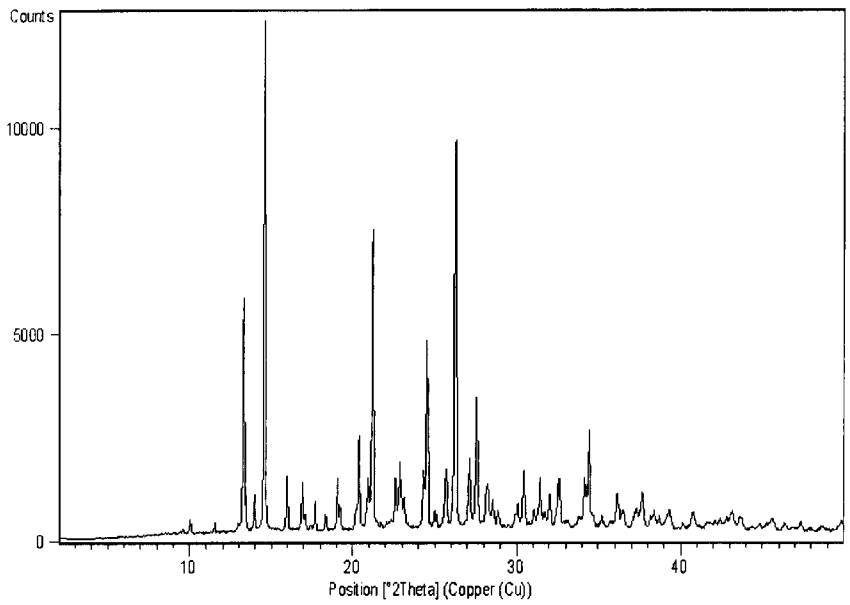
(54) Title: NOVEL FORM OF RANELIC ACID




[Fig 1]

(57) Abstract: The present invention relates to an unsolvated form of ranelic acid and the process for the preparation thereof.

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**Declarations under Rule 4.17**:

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— *of inventorship (Rule 4.17(iv))*

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— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

PRIORITY

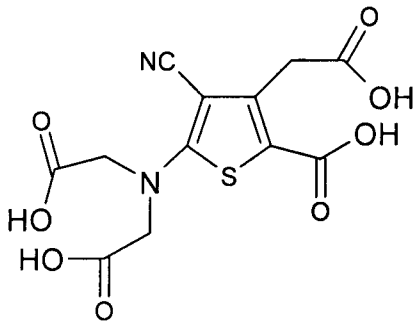
[0001] This application claims the benefit of IN 2801/MUM/2010 filed on October 8, 2010, the content of which is incorporated herein by reference.

FIELD OF INVENTION

[0002] The present invention relates to an unsolvated form of ranelic acid and the process for the preparation thereof.

BACKGROUND OF THE INVENTION.

[0003] Ranelic acid is represented by the structure:




I

[0004] Ranelic acid is an intermediate used in the synthesis of strontium ranelate.

[0005] Strontium ranelate is the bis strontium (II) salt of ranelic acid and is used in the treatment of osteoporosis.

[0006] United States Patent No. 5128367 (the US'367 patent) discloses ranelic acid and process for preparing ranelic acid. The US'367 patent provides a process for preparation of ranelic acid starting from tetraester involving heating the tetraester at reflux in the presence of sodium hydroxide in an aqueous alcoholic medium, followed by hydrolysis using a sulfonic acid resin. The residue is recrystallized to obtain ranelic acid.

[0007] The known methods may involve the use of expensive resins and crystallization operations, and the subsequent low yield reported as low as 70%.

[0008] There remains a need to provide a process for a more direct preparation of pure ranelic acid, which results in good yield and high purity, from a reaction, which is cost effective, thus minimizing additional operations for treatment such as crystallization, purification.

SUMMARY OF THE INVENTION

[0009] The present invention relates to an unsolvated form of ranelic acid.

[0010] The present invention relates to novel form of ranelic acid hydrate wherein the compound exhibits at least any one of the following characteristics :

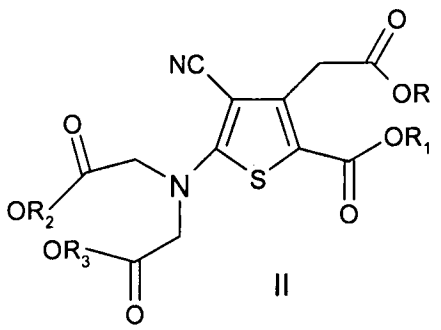
a) X-ray powder diffraction having characteristic peaks expressed in degrees 2Θ ±0.2° at about 13.3, 14.59, 21.19, 24.42, 26.24, 34.42;

b) DSC thermogram having one endothermic peak at 78.39°C and another peak at 154.68°C.

c) TGA thermogram showing a weight loss of about 9.39 percent up to a temperature of 100°C.

[0011] The present invention provides a process for the preparation of ranelic acid comprising:

a) reacting a tetraester of formula II



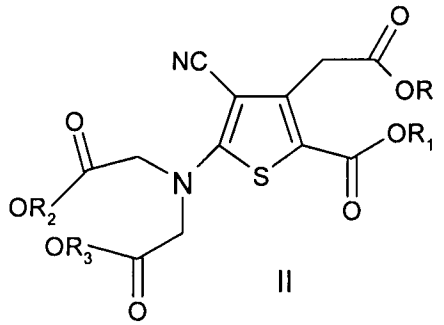

II

wherein R, $R_1$, $R_2$, and $R_3$ are independently a linear or branched C1-C6 alkyl group or a substituted or unsubstituted C3-C12 cyclic group, with a base in a solvent to obtain a reaction mixture; and

b) subjecting the reaction mixture to treatment with an acid to precipitate ranelic acid.

[0012] In yet another embodiment, the present invention provides a process for the preparation of ranelic acid comprising :

a) reacting a tetraester of formula II




II

wherein R, $R_1$, $R_2$, and $R_3$ are independently a linear or branched C1-C6 alkyl group or a substituted or unsubstituted C3-C12 cyclic group, with a base in a solvent to obtain a reaction mixture; and

b) subjecting the reaction mixture to treatment with acid to adjust pH of reaction mixture to 1 or less than 1.

[0013] In one embodiment, the present invention provides a process for preparation of strontium ranelate comprising reacting ranelic acid with strontium salt in the presence of a base.

[0014] In another embodiment, the present invention provides a process for purifying strontium ranelate comprising treating strontium ranelate with an organic acid and or water.

[0015] The present invention provides strontium ranelate containing lithium content less than 60 ppm.

BRIEF DESCRIPTION OF DRAWINGS

[0016] Fig. 1 represents an XRD diffractogram of ranelic acid of the present invention

[0017] Fig. 2 represents a DSC thermogram of ranelic acid of the present invention

[0018] Fig. 3 represents a TGA thermogram of ranelic acid of the present invention

[0019] Fig. 4 represents an XRD diffractogram of amorphous strontium ranelate of the present invention.

[0020] Fig. 5 represents TGA of amorphous strontium ranelate of the present invention.

## DETAILED DESCRIPTION OF THE INVENTION

[0021] The present invention relates to an unsolvated form of ranelic acid. Ranelic acid is a useful intermediate in the preparation of strontium ranelate.

[0022] The term "unsolvated" refers to the absence of a complex of ranelic acid with one or more pharmaceutically acceptable solvent molecules, for example tetrahydrofuran, ethanol, acetone and the like.

[0023] The term hydrate refers to complex with water molecule.

[0024] The present invention relates to a novel hydrate form of ranelic acid characterized by at least one of the following:

a) X-ray powder diffraction patterns having characteristic peaks expressed in degrees 2Θ ±0.2° at about 13.3, 14.59, 21.19, 24.42, 26.24, 34.42;

b) DSC thermogram having one endothermic peak at 78.39°C and another peak at 154.68°C; and

c) TGA thermogram showing a weight loss of about 9.39 percent up to a temperature of 100°C.

[0025] X-Ray Powder were performed on ARL X-Ray Diffractometer model XPERT-PRO (PANalytical) scanning parameters start position [°2Th.] 2.01 and end position [°2Th.] 49.98.

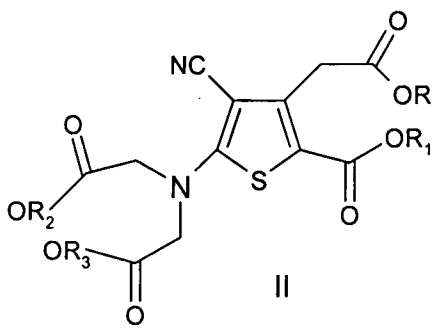
[0026] Ranelic acid is further characterized by DSC thermogram having two endothermic peaks one at 78.39°C and another peak at 154.68°C.

[0027] Ranelic acid is further characterized by differential scanning calorimetry (DSC) with five endothermic curves. The first endothermic curve is at about 78.39°C and onset of 50.79°C and endset of 94.38°C. The second endothermic curve is at about 131.91°C and onset of 119.75°C and endset of 138.04°C.The third endothermic curve is at about 154.68°C and onset of 144.67°C and endset of 160.10°C. The fourth endothermic curve is at about 169.20°C and onset of about 163.78°C and endset of about 174.94°C and the fifth curve is at 178.34°C with an onset of about 177.23°C and an endset of about 179.55°C. The DSC thermogram, which is substantially in accordance with Fig 2, is measured by a Differential Scanning Calorimeter (DSC 822, Mettler Toledo) at a scan rate of $10^0$C per minute with an Indium standard.

[0028] The present invention further characterizes the novel form by thermogravimetric analysis, (TGA) thermogram, which is substantially in accordance with Fig.3, shows a weight loss of about 9.39 percent up to a temperature of about 100°C and recorded on a TGA Q500 V 20.6 in a platinum pan with a temperature rise of about $10^0$C per minute in the range of about $30^0$C to about $350^0$C.

[0029] The present invention provides a process for the preparation of ranelic acid comprising:

a) reacting a tetraester of formula II




II

wherein R, $R_1$, $R_2$, and $R_3$ are independently a linear or branched C1-C6 alkyl group or a substituted or unsubstituted C3-C12 cyclic group, optionally susbstituted benzyl in the presence of a base in a solvent to obtain a reaction mixture; and

b) subjecting the reaction mixture to treatment with an acid to precipitate ranelic acid.

**[0030]** The term "linear or branched C1-6 alkyl" includes groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, ter-butyl, n-pentyl. The term C3-C12 cyclic group includes groups such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl.

**[0031]** The term "substituted C3-C12 cycloalkyl" includes groups which have replaced hydrogen atom to any carbon of the cycloalkyl with a halogen, alkyl, substituted alkyl, aryl.

**[0032]** The term "optionally substituted benzyl" means benzyl which is optionally substituted with halo, alkyl, alkoxy or nitro group wherein halo includes Cl, Br, I; alkyl includes methyl, ethyl, propyl, butyl; alkoxy includes methoxy, ethoxy, propoxy.

**[0033]** In a) of the process above, the solvent is selected from the group consisting of water, water miscible solvents and mixtures thereof. Water miscible solvents include cyclic ether such as tetrahydrofuran, 1,4-dioxane, nitrile such as acetonitrile, and ketones such as acetone, methyl isobutyl ketone. Preferably the solvent is a mixture of water and tetrahydrofuran.

**[0034]** The base is selected from the group consisting of inorganic base such as lithium carbonate, lithium hydroxide monohydrate, calcium hydroxide, cesium hydroxide and mixtures thereof. Preferably, the base is lithium hydroxide monohydrate.

**[0035]** The addition of base results in an exothermic reaction. The addition is therefore carried out over a period of about 45 minutes to about 1 hour. The reaction time can vary from between 20 hours to about 30 hours. Preferably, the reaction transpires between 21 hours to 23 hours.

**[0036]** The reaction is carried out at a temperature of about 0°C to about 30°C. Preferably the reaction is carried out at temperature of about 5°C to about 10°C.

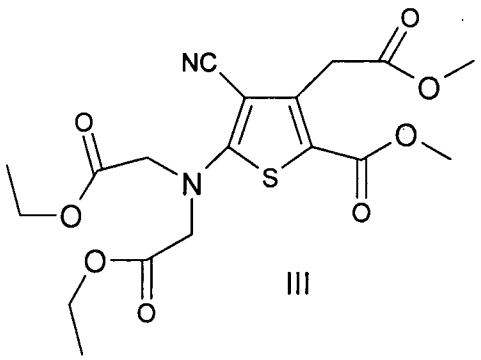
[0037] In b) of the process above, acids are selected from strong acids selected from the group of mineral acids such as sulphuric acid, phosphoric acid, hydrochloric acid and organic acids such as methane sulfonic acid, trifluoromethane sulfonic acid. Preferably the acid is sulfuric acid.

[0038] The reaction mixture is stirred for about 30 minutes to about 1 hour. Preferably, the reaction mixture is stirred for about 30 minutes.

[0039] Solid ranelic acid is isolated by methods known in the art such as filtration concentration, centrifugation and the like.

[0040] In preferred embodiment, the present invention relates to a process of preparation of novel unsolvated form of ranelic acid comprising:

a) reacting methyl 5-[bis(2-ethoxy-2-oxoethyl) amino]-4-cyano-3-(2-methoxy-2-oxoethyl)-2-thiophenecarboxylate, compound of formula III, in tetrahydrofuran,




III

with an aqueous solution of lithium hydroxide to obtain a reaction mixture; and
b) subjecting the reaction mixture to treatment with sulfuric acid.

[0041] In a) of the immediate process above, methyl 5-[bis(2-ethoxy-2-oxoethyl) amino]-4-cyano-3-(2-methoxy-2-oxoethyl)-2-thiophenecarboxylate, compound of formula III is dissolved in tetrahydrofuran.

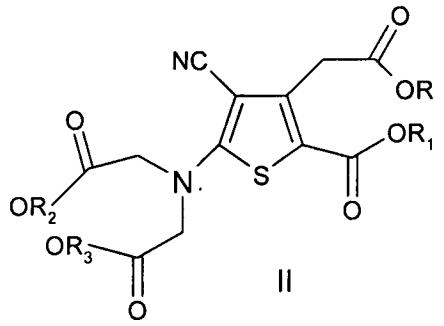
[0042] The above solution is cooled to a temperature of about 0°C to about 20°C. Preferably the solution is cooled to a temperature of about 5°C to about 10°C and at

this temperature a solution lithium hydroxide is added slowly. The reaction is stirred and maintained for about 15 hours to about 30 hours. Preferably the reaction is stirred and maintained for about 18 hours to about 23 hours.

[0043] In b) of the process above, the reaction mixture is acidified using 10% sulfuric acid and the product from the reaction mixture is filtered or extracted into a suitable solvent selected from ethylacetate, methyl ethyl ketone, methyl isobutyl ketone, methyl tertiary butyl ether. Preferably the ranelic acid is extracted with ethyl acetate.

[0044] Solid ranelic acid is isolated by methods known in the art such as filtration, concentration, centrifugation and the like.

[0045] In one embodiment, the present invention provides a process of preparation of ranelic acid comprising: a) reacting a tetraester of formula II

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wherein R, R1, R2, and R3 are independently a linear or branched C1-C6 alkyl group or a substituted or unsubstituted C3-C12 cyclic group, in the presence of a base in a solvent to obtain a reaction mixture; and

b) subjecting the reaction mixture to treatment with acid to adjust pH of reaction mixture to 1 or less than 1.

wherein R, R1, R2, and R3 are as described above.

[0046] In a) of the immediate process above, the reaction may be carried out as described previously in the earlier sections.

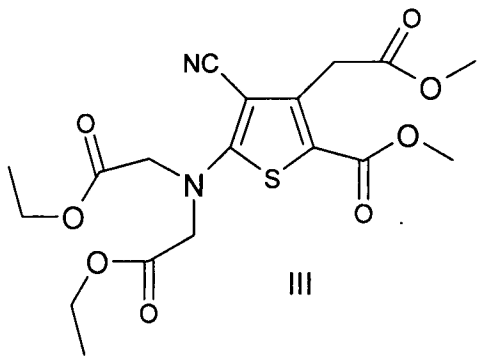
[0047] The process in b) above, a solution of sulfuric acid is added to obtain a pH of less than 1.

[0048] It has been surprisingly found that although the product precipitates at acidic pH, maximum precipitation occurs by adjusting pH to about 1 or about less than 1. The acidic reaction mixture is stirred for about 30 minutes to about 1 hour. Preferably the reaction mixture is stirred for about 30 minutes. Ranelic acid is filtered or extracted into a

suitable solvent selected from ethylacetate, methyl ethyl ketone, methyl isobutyl ketone, methyl tertiary butyl ether. Preferably ranelic acid is extracted with ethyl acetate.

**[0049]** In a preferred embodiment, the present invention relates to a process of preparation of ranelic acid comprising:

a) reacting methyl 5-[bis(2-ethoxy-2-oxoethyl) amino]-4-cyano-3-(2-methoxy-2-oxoethyl)-2-thiophenecarboxylate, compound of formula III, in tetrahydrofuran,




III

with an aqueous solution of lithium hydroxide to obtain a reaction mixture; and

b) subjecting the reaction mixture to treatment with sulfuric acid to adjust pH of reaction mixture to less than 1.

**[0050]** The process in a) involves preparation of a solution of methyl 5-[bis(2-ethoxy-2-oxoethyl) amino]-4-cyano-3-(2-methoxy-2-oxoethyl)-2-thiophenecarboxylate, of formula III in tetrahydrofuran . An aqueous solution of lithium hydroxide is added to the above ester solution. The addition is carried out at a temperature of about 5-10°C.

**[0051]** The process in b) involves addition of sulfuric acid. The addition is carried out to adjust the pH of the solution to about less than 1. The precipitated ranelic acid is isolated by filtration, centrifugation or extraction. Preferably the precipitated ranelic acid is extracted and isolated.

**[0052]** The product was isolated at different acidic pH's and the analysis is as shown in Table 1.

**Table 1**

| pH | Input reaction mass | Output |
|---|---|---|
| 1 | 40 ml | 7.4 gm |

| | | |
|---|---|---|
| 1.5 | 40 ml | 5.5 gm |
| 2 | 40 ml | 3.7 gm |
| 3 | 40 ml | 0.5 gm |

[0053] Ranelic acid obtained by the present invention is an unsolvated form and has purity greater than 98%.

[0054] Preferably ranelic acid obtained by the present invention has purity greater than 99%.

[0055] In one embodiment, the novel form of ranelic acid obtained is a hydrate and is stable at room temperature.

[0056] The ranelic acid obtained by the present invention can serve as a useful intermediate in the preparation of active pharmaceutical ingredient.

[0057] In one embodiment, the present invention provides process for the preparation of strontium ranelate from ranelic acid, comprising reacting ranelic acid with strontium salt in the presence of a base.

[0058] In one embodiment the ranelic acid used is the isolated solid form. Preferably hydrate of ranelic acid.

[0059] The above reaction may be carried out in presence of water or alcoholic solvents such as methanol. Preferably the solvent is water.

[0060] The base may be selected from inorganic or organic bases such as hydroxides such as sodium hydroxide, potassium hydroxide, lithium hydroxide, carbonates such as sodium carbonate lithium carbonate, potassium carbonate, bicarbonates such as sodium bicarbonate, potassium bicarbonate. Preferably the inorganic base is lithium hydroxide. The organic bases may be selected from the group consisting of pyridine, picoline, quinoline, piperdine, pyrrolidine, N-methylmorphline, amine such

as triethylamine and diisopropyl amine and combination thereof. Preferably the base is lithium hydroxide.

[0061] The strontium salt may be selected from strontium chloride, strontium bromide, strontium sulfate, strontium acetate, strontium carbonate, strontium oxalate, strontium nitrate and a mixture thereof. Preferably the strontium salt is strontium chloride hexahydrate.

[0062] The above reaction mixture is stirred for a period of about 10 hours to about 30 hours. Preferably, the reaction mixture is stirred for about 15 hours to about 20 hours. The reaction transpires at a temperature of about 25°C to about 30°C. The precipitate of distrontium salt of 5-[bis (carboxymethyl) amino]-2-carboxy-4-cyano-3-thiopheneacetic acid octahydrate can be isolated by techniques known in the art such as filtration, centrifugation.

[0063] In one embodiment, the present invention provides process for the preparation of amorphous strontium ranelate from ranelic acid, comprising reacting ranelic acid with anhydrous strontium salt in the presence of base.

[0064] In one embodiment, the ranelic acid used is the unsolvated form. Preferably hydrate of ranelic acid.

[0065] The base may be selected from inorganic or organic bases such as hydroxides, carbonates, bicarbonates. Preferably the inorganic base is lithium hydroxide. The organic bases may be selected from the group consisting of amine, pyridine, picoline, quinoline, piperidine, pyrrolidine, N-methylmorphline, and combination thereof. Preferably the base is diisopropyl amine.

[0066] The above reaction may be carried out in presence of water miscible solvents for example alcoholic solvents such as methanol, ethanol, isopropanol and the like. Preferably the solvent is methanol.

[0067] The strontium salt may be selected from strontium chloride, strontium bromide, strontium sulfate, strontium acetate, strontium carbonate, strontium oxalate, strontium nitrate and a mixture thereof. Preferably the strontium salt is strontium chloride anhydrous.

[0068] In a preferred embodiment, strontium chloride anhydrous is dissolved in methanol and to this diisopropyl amine is added. Then this solution is added to a solution of ranelic acid in methanol. The reaction is stirred and maintained for a period of about 30 hours to about 50 hours. Preferably the reaction is stirred and maintained for about 45 hours to 49 hours.

[0069] The precipitate of distrontium salt of 5-[bis (carboxymethyl) amino]-2-carboxy-4-cyano-3-thiopheneacetic acid can be isolated by techniques known in the art such as filtration, centrifugation.

[0070] In one embodiment, amorphous strontium ranelate is characterized by an X-ray diffraction pattern, substantially in accordance with Fig. 4.
In one embodiment amorphous strontium ranelate is characterized by thermogravimetric analysis, (TGA) thermogram, which is substantially in accordance with Fig 5., shows a weight loss of 14.5 percent up to a temperature of about 150°C and recorded on a TGA Q500 V 20.6 in a platinum pan with a temperature rise of about $10^0$C per minute in the range of about 30°C to about 350°C.

[0071] In one embodiment, the present invention relates to a process for purification of strontium ranelate comprising treatment of strontium ranelate with water or an organic

acid, for example, acetic acid, lactic acid, malonic acid, tartaric acid, oxalic acid or a mixture thereof. Preferably, the acid is oxalic acid, advantageously to be used as 1% aqueous solution.

[0072] The purification can be carried out preferably by subjecting to a slurrying step carried out at temperature between the range of about 15°C to about 40°C, preferably at about 20°C to about 30°C resulting into removal of lithium.

[0073] In one embodiment, the present invention relates to strontium ranelate containing lithium content less than 60 parts per million (ppm).

[0074] In one embodiment, the present invention relates to strontium ranelate containing lithium content less than 20 parts per million (ppm).

[0075] In one embodiment, the present invention relates to strontium ranelate containing lithium content less than 10 parts per million (ppm).

[0076] Strontium ranelate obtained from ranelic acid of the present invention has purity greater than 99.0% as measured by high performance liquid chromatography (HPLC).

[0077] While the present invention has been described in terms of its specific embodiments, certain modifications and equivalents will be apparent to those skilled in the art and are intended to be included within the scope of the present invention.

[0078] The examples that follow, are not intended to be limiting of the scope of the present invention but read in conjunction with the detailed and general description above, to provide further understanding of the present invention and an outline of processes for preparation.

EXAMPLES:

**Example 1** Preparation of ranelic acid.

[0079] In a 2 lit 4-neck round bottom flask equipped with overhead stirrer, double surface condenser, thermowel pocket placed in oil bath a solution of methyl 5-[bis(2-ethoxy-2-oxoethyl) amino]-4-cyano-3-(2-methoxy-2-oxoethyl)-2-thiphene-carboxy-late (150g,0.35 mol) was prepared in tetrahydrofuran (450ml). Slowly a solution of lithium hydroxide (66.0 g in 600 ml water) is added to the above solution of ester at about 5-10°C. The reaction mass was stirred for about 22 hours at about 5-10°C. The two layers formed were separated. The lower layer was acidified with 10% sulfuric acid to bring the pH to about less than 1. The reaction mass was further stirred for about 30 minutes. Then the reaction mass was extracted with ethyl acetate. Ethyl acetate layers were pooled and distilled to obtain solid ranelic acid.

Dry weight of ranelic acid 115 g (Yield: 95%, HPLC purity: 99.12%), melting range: 146.4°C to 147.4°C; TGA: weight loss of 9.39 percent upto a temperature of 100°C.

[0080] **Example 2** Preparation of 5-[bis (carboxymethyl) amino]-2-carboxy-4-cyano-3-thiopheneacetic acid distrontium salt

In a 500 ml 4-neck round bottom flask equipped with overhead stirrer, double surface condenser, thermowel pocket placed in oil bath, a solution of ranelic acid (5 g) in water (45 ml) was prepared. To this solution, 10% w/v aqueous lithium hydroxide solution (27.5 ml) was added and the reaction mass was stirred at about 25-30°C. A solution of strontium chloride hexahydrate (8.57 g) in water (85 ml) was added to the above solution at about 25-30 °C. This reaction mixture was stirred for about 15 hours to about 20 hours at about 25-30°C. The precipitated solid, distrontium salt of 5-[bis (carboxymethyl) amino]-2-carboxy-4-cyano-3-thiopheneacetic acid was filtered and washed with water. The resulting wet material was dried at about 30-35 °C under reduced pressure. Yield 7.8 g of strontium ranelate octahydrate. purity > 99.0% as determined by HPLC.

Strontium ranelate octahydrate (50 g) was suspended in purified water (500 ml), and the contents were stirred at 25-30 °C for 10 min. To this 1.0% oxalic acid (0.5 g) was added and the content was stirred for 4.0 h at 25-30°C. The product was filtered and

washed with purified water. The wet cake was added into purified water and the content was stirred for 1.0 h at 25-30°C. The product was filtered and washed with purified water. The product was dried at 30°C -35°C under reduced pressure (~20mm Hg) to obtain 45g of strontium ranelate (0.9 w/w based on strontium ranelate octahydrate). Li content< 13 ppm. Loss on drying not more than 23.5%, HPLC purity>99%.

[0081] **Example 3** Preparation of amorphous 5-[bis (carboxymethyl) amino]-2-carboxy-4-cyano-3-thiopheneacetic acid distrontium salt.

In a 250ml 4-neck round bottom flask equipped with overhead stirrer, double surface condenser, thermowel pocket placed in oil bath a solution of anhydrous strontium chloride (4.63gm) was prepared in methanol (150ml) under nitrogen atmosphere. To this diisopropyl amine was added and the reaction mass was stirred for 15 minutes. The above reaction mass was added to a solution of ranelic acid (5gm) in methanol. The reaction was stirred for 48 hours and the precipitated product was filtered and washed with methanol under nitrogen atmosphere. The product was dried at about 35-40°C under reduced pressure (~10mm Hg) to obtain 3.9gm of amorphous strontium ranelate. HPLC purity>98%, TGA: weight loss of 14.5 percent upto a temperature of 150°C.

**Claims:**

1. Unsolvated solid ranelic acid.

2. The compound of claim 1, wherein the compound is a hydrate and is characterized by at least any one of the following:

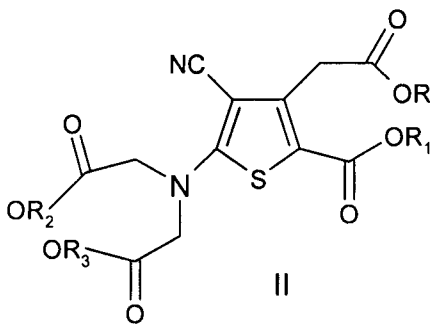
a) XRD powder diffraction pattern having characteristics peaks expressed in degrees 2Θ ±0.2° at about 13.3, 14.59, 21.19, 26.24;

b) DSC thermogram having one endothermic peak at 78.39°C and another peak at 154.68°C; and

c) TGA thermogram showing a weight loss of about 9.39 percent up to a temperature of 100°C.

3. A process for the preparation of ranelic acid comprising:

a) reacting a tetraester of formula II




II

wherein R, $R_1$, $R_2$, and $R_3$ are independently a linear or branched C1-C6 alkyl group or a substituted or unsubstituted C3-C12 cyclic group, with a base in a solvent to obtain a reaction mixture; and

b) subjecting the reaction mixture to treatment with an acid to precipitate ranelic acid.

4. The process of claim 3, wherein R, $R_1$, $R_2$, and $R_3$ of the tetraester of Formula II are independently a linear or branched $C_1$-$C_6$ alkyl group.

5. The process of claim 3, wherein R, $R_1$, $R_2$, and $R_3$ of the tetraester of Formula II are independently methyl or ethyl.

6. The process of claim 3, wherein R, $R_1$, $R_2$, and $R_3$ of the tetraester of Formula II are ethyl.

7. The process of claim 3, wherein the base is an inorganic base such as hydroxide base selected from the group consisting of lithium hydroxide, lithium carbonate, lithium hydroxide monohydrate, calcium hydroxide, cesium hydroxide and mixtures thereof.

8. The process of claim 3, wherein the solvent is selected from the group consisting of water, water miscible organic solvent and mixtures thereof.

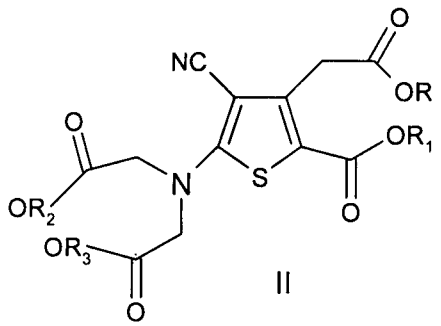
9. The process of claim 3, wherein the water miscible organic solvent is selected from the group consisting of cyclic ether, water, ketone, nitrile and mixtures thereof.

10. The process of claim 3, wherein acid is a mineral acid selected from sulfuric acid, hydrochloric acid, hydrobromic acid.

11. The process of claim 9 wherein the cyclic ether is tetrahydrofuran, dioxane and mixtures thereof.

12. A process of precipitating ranelic acid comprising:

a) reacting a tetraester of formula II




II

wherein R, $R_1$, $R_2$, and $R_3$ are independently a linear or branched C1-C6 alkyl group or a substituted or unsubstituted C3-C12 cyclic group, with a base in a solvent to obtain a reaction mixture;

and

b) subjecting the reaction mixture to treatment with acid to adjust pH of reaction mixture to 1 or less than 1.

13. The process of claim 3 wherein ranelic acid has purity greater than 98%.

14. The process of claim 13 wherein ranelic acid has purity greater than 99%.

15. A process for preparation of strontium ranelate comprising reacting ranelic acid with strontium salt in the presence of a base.

16. A process for purifying strontium ranelate comprising treating strontium ranelate with an organic acid and or water.

17. The process of claim 16, wherein the ranelic acid is isolated solid ranelic acid.

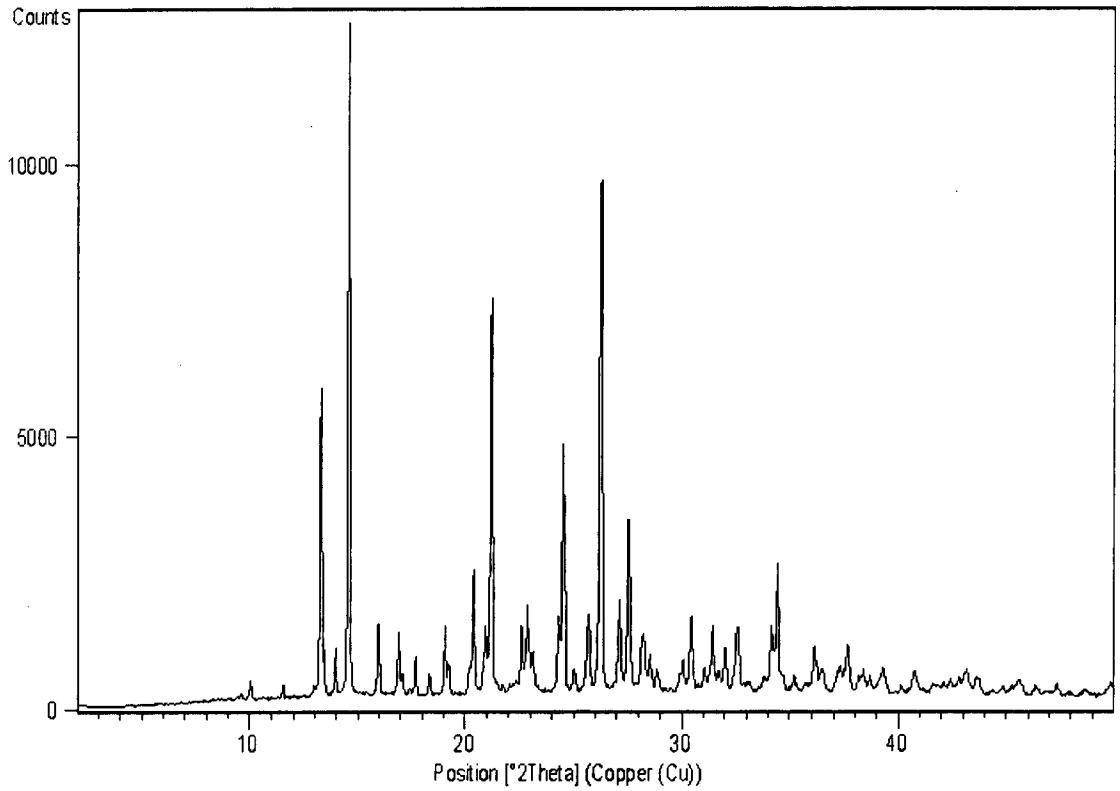
18. Strontium ranelate containing lithium content less than 60 ppm.

19. The compound of claim 1 characterized by at least any one of the following:

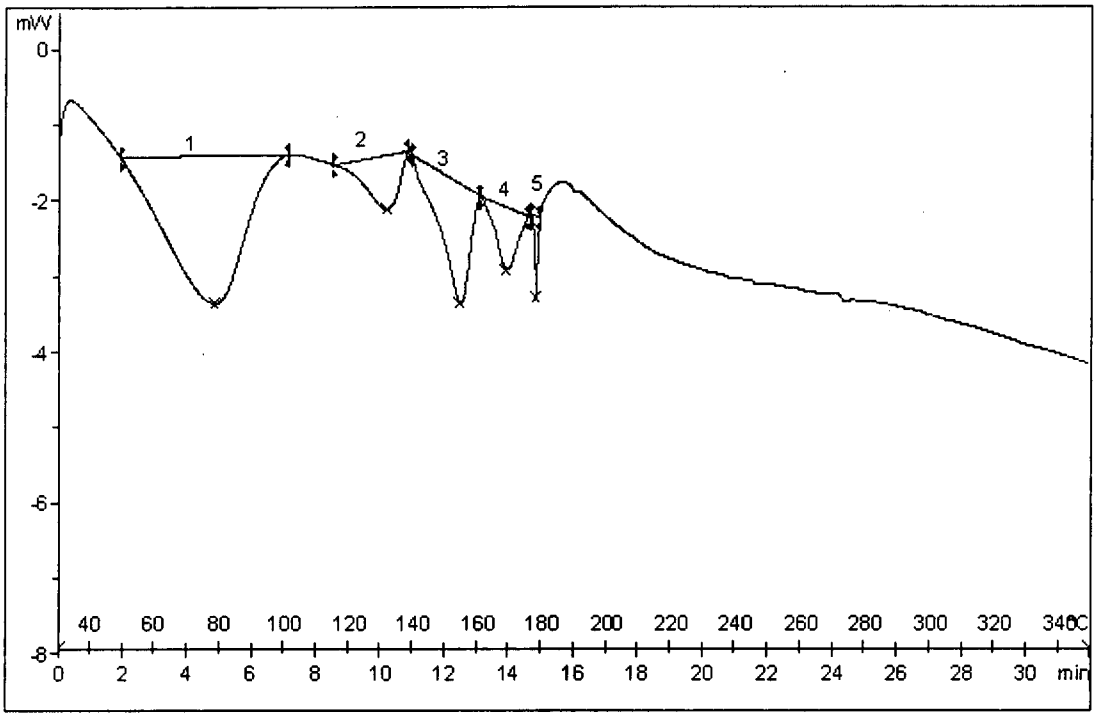
a) XRD characterized by XRD pattern, substantially in accordance with Fig. 1;

b) DSC thermogram substantially in accordance with Fig.2;

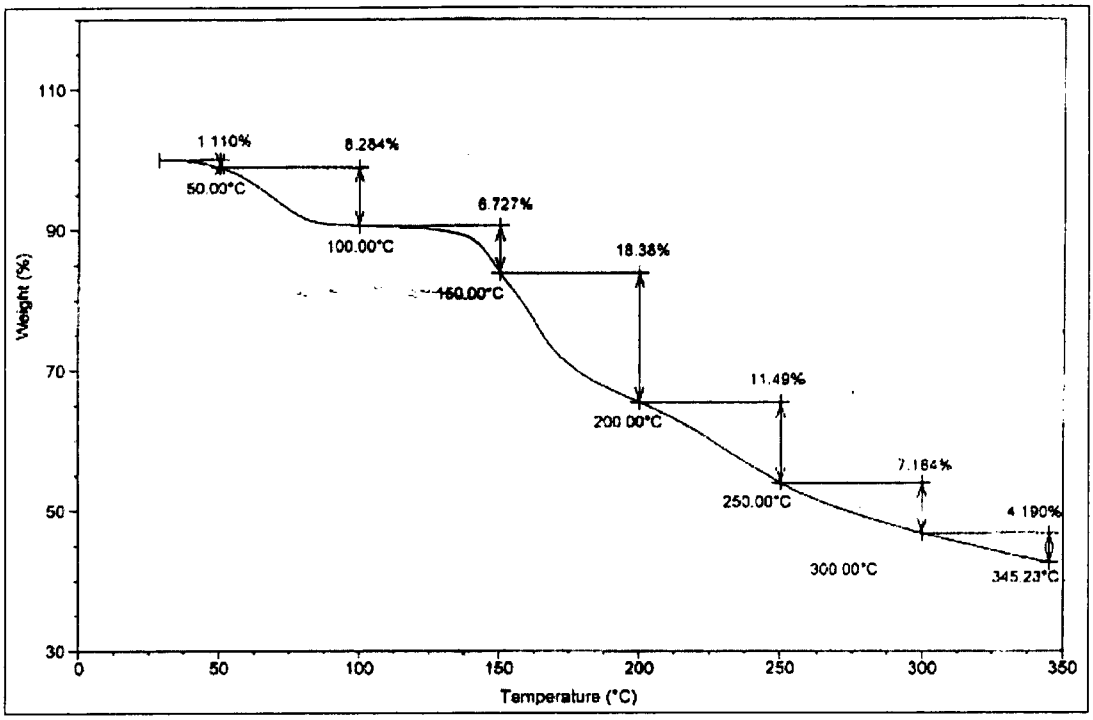
c) TGA thermogram, substantially in accordance with Fig.3.



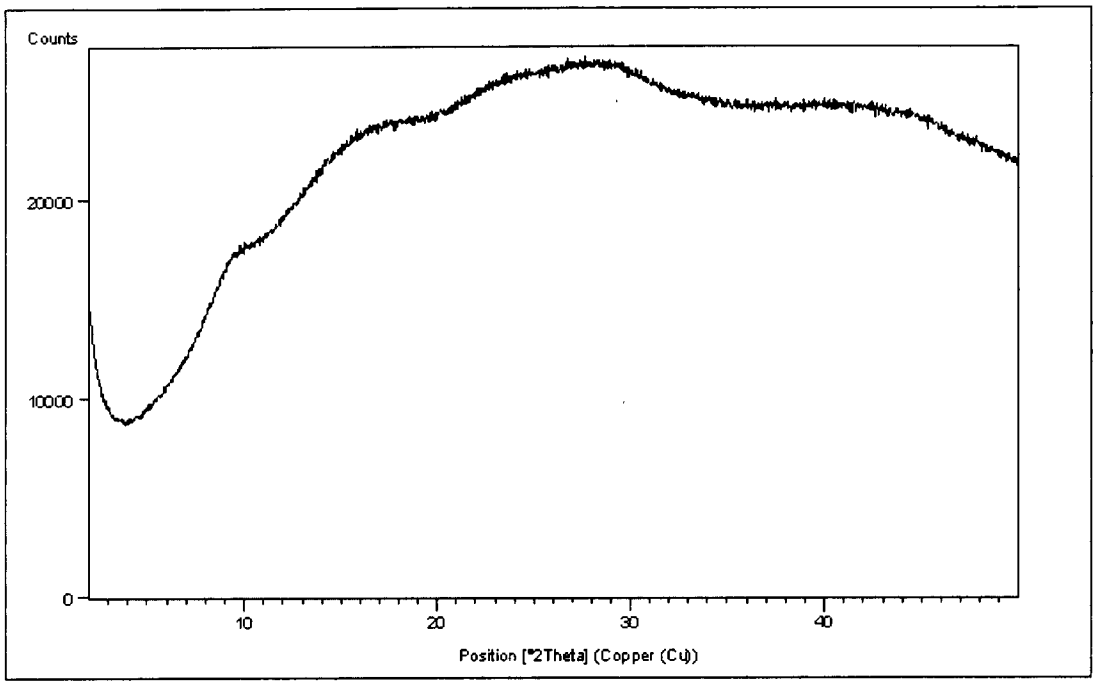

[Fig 1]


mV
0
-2
-4
-6
-8
1
2
3
4
5
40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340C
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 min

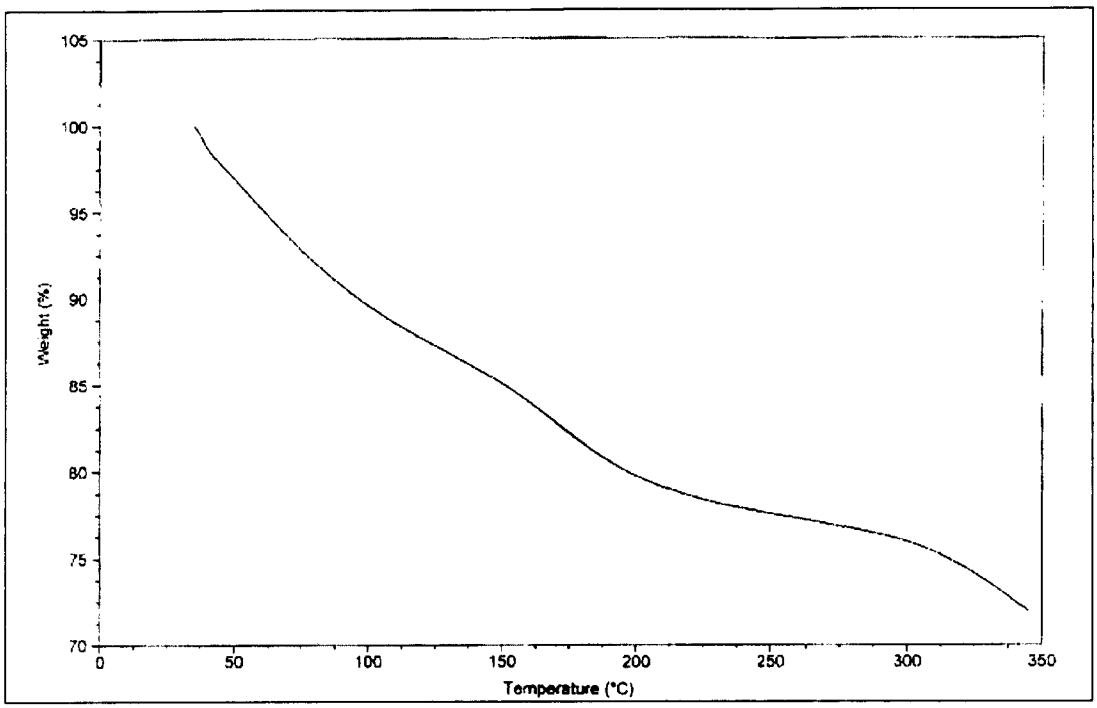
[Fig 2]


110
90
70
50
30
Weight (%)
0
50
100
150
200
250
300
350
Temperature (°C)
1.110%
8.284%
50.00°C
100.00°C
6.727%
18.38%
150.00°C
11.49%
200.00°C
250.00°C
7.184%
4.190%
300.00°C
345.23°C

[Fig 3]




[Fig 4]


105
100
95
90
85
80
75
70
Weight (%)
0
50
100
150
200
250
300
350
Temperature (°C)

[Fig 5]