Patent claims

1. Crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride,

which crystalline (2R,S)-DOTAP chloride has one of the following characteristics:
2 theta values comprising at least values of about 12.6, about 19.5, about 20.2, about 21.5 and about 25.2; or
2 theta values comprising at least values of about 6.5, about 12.6, about 13.4, about 19.5, about 20.2, about 21.5, about 25.2 and about 29.8; or
an X-ray powder diffraction pattern corresponding to the pattern depicted in Fig. 1;

or

which crystalline (2S)-DOTAP chloride has one of the following characteristics:
2 theta values comprising at least values of about 12.8, about 19.5, about 19.8, about 20.2, and about 21.6;
2 theta values comprising at least values of about 6.5, about 12.8, about 19.5, about 19.8, about 20.2, about 20.7, about 21.6 and about 25.3; or
an X-ray powder diffraction pattern corresponding to the pattern depicted in Fig. 2;

or

which crystalline (2R)-DOTAP chloride has one of the following characteristics:
2 theta values comprising at least values of about 12.8, about 19.5, about 19.8, about 20.3, and about 21.6;
2 theta values comprising at least values of about 6.6, about 12.8, about 19.5, about 19.8, about 20.3, about 20.8, about 21.6 and about 25.3; or
an X-ray powder diffraction pattern corresponding to the pattern depicted in Fig. 3.

2. Crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride, which has a stability of higher than 99% by weight and Area-% determined by HPLC when stored at 25°C for 36 months or at 40°C for 12 months.

3. Crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride, which has a chemical purity of at least about 95% determined by HPLC.

4. Crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride according to one or more of claims 1 to 3, which has a melting point of higher than 160°C and a melting enthalpy of more than -130 J/g.

5. A pharmaceutical composition comprising crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride according to one or more of claims 1 to 4 and a pharmaceutically acceptable carrier.

6. A pharmaceutical composition according to claim 5, further comprising one or more peptides, nucleotides, antigenes, cytostatic agents, liposomes, lipoplexes, nanoparticles or microemulsions, or a mixture thereof.

7. A process for preparing a crystalline form of (2R,S)-, (2S)- or (2R)-DOTAP chloride according to one or more of claims 1 to 4, comprising crystallizing (2R,S)-, (2S)- or (2R)-DOTAP chloride from one or more aprotic solvents.

8. A process according to claim 7, wherein the one or more aprotic solvents comprise one or more protic solvents.

9. A process according to claim 7 or 8, wherein the crystallizing takes place under an inert atmosphere.

10. A process according to one or more of claims 7 to 9, wherein the crystallizing takes place by slow cooling at a rate of 0.001°C to 0.1°C per minute for 5 to 200 hours.

11. A process according to claim 10, wherein slow cooling is for a time period of about 10 to 100 hours.

12. A process according to one or more of claims 7 to 11, where crystallisation is carried out directly from a reaction solution without prior purification, which reaction solution is from a process of preparing (2R,S)-, (2S)- or (2R)-DOTAP chloride.

13. A process according to one or more of claims 7 to 12, which further comprises a recrystallization of crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride.

14. Crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride obtainable by a process according to one or more of claims 7 to 13.

15. A method of transfecting a cell in vitro, comprising administering to said cell a crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride according to one or more of claims 1 to 4.

16. Use of a crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride according to one or more of claims 1 to 4 in the manufacture of a cell transfecting medicament for the treatment of a disease.

17. Use as claimed in claim 16 wherein the disease is cancer.

Claims

1. Crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride,
which crystalline (2R,S)-DOTAP chloride has one of the following characteristics:
2 theta values comprising at least values of about 12.6, about 19.5, about 20.2, about 21.5 and about 25.2; or
2 theta values comprising at least values of about 6.5, about 12.6, about 13.4, about 19.5, about 20.2, about 21.5, about 25.2 and about 29.8; or an X-ray powder diffraction pattern corresponding to the pattern depicted in Fig. 1;
or
which crystalline (2S)-DOTAP chloride has one of the following characteristics:
2 theta values comprising at least values of about 12.8, about 19.5, about 19.8, about 20.2, and about 21.6;
2 theta values comprising at least values of about 6.5, about 12.8, about 19.5, about 19.8, about 20.2, about 20.7, about 21.6 and about 25.3; or an X-ray powder diffraction pattern corresponding to the pattern depicted in Fig. 2;
or
which crystalline (2R)-DOTAP chloride has one of the following characteristics:
2 theta values comprising at least values of about 12.8, about 19.5, about 19.8, about 20.3, and about 21.6;
2 theta values comprising at least values of about 6.6, about 12.8, about 19.5, about 19.8, about 20.3, about 20.8, about 21.6 and about 25.3; or an X-ray powder diffraction pattern corresponding to the pattern depicted in Fig. 3.

2. Crystalline (2R.S)-, (2S)- or (2R)-DOTAP chloride, as claimed in claim 1, which has a stability of higher than 99% by weight and Area-% determined by HPLC when stored at 25°C for 36 months or at 40°C for 12 months.

3. Crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride as claimed in claim 1, which has a chemical purity of at least about 95% determined by HPLC.

4. Crystalline (2R.S)-, (2S)- or (2R)-DOTAP chloride according to one or more of claims 1 to 3, which has a melting point of higher than 160°C and a melting enthalpy of more than -130

J/g.

5. A pharmaceutical composition comprising crystalline (2R,S)-, (2S)-or (2R)-DOTAP chloride according to one or more of claims 1 to 4 and a pharmaceutically acceptable carrier.

6. A pharmaceutical composition according to claim 5, further comprising one or more peptides, nucleotides, antigenes, cytostatic agents, liposomes, lipoplexes, nanoparticles or microemulsions, or a mixture thereof.

7. A process for preparing a crystalline form of (2R,S)-, (2S)- or (2R)-DOTAP chloride according to one or more of claims 1 to 4, comprising crystallizing (2R,S)-, (2S)- or (2R)-DOTAP chloride from one or more aprotic solvents.

8. A process according to claim 7, wherein the one or more aprotic solvents comprise one or more protic solvents.

9. A process according to claim 7 or 8, wherein the crystallizing takes place under an inert atmosphere.

10. A process according to one or more of claims 7 to 9, wherein the crystallizing takes place by slow cooling at a rate of 0.001 °C to 0.1 °C per minute for 5 to 200 hours.

11. A process according to claim 10, wherein slow cooling is for a time period of about 10 to 100 hours.

12. A process according to one or more of claims 7 to 11, where crystallisation is carried out directly from a reaction solution without prior purification, which reaction solution is from a process of preparing (2R,S)-, (2S)- or (2R)-DOTAP chloride.

13. A process according to one or more of claims 7 to 12, which further comprises a recrystallization of crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride.

14. A method of transfecting a cell in vitro, comprising administering to said cell a crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride according to one or more of claims 1 to 4.

15. Use of a crystalline (2R,S)-, (2S)- or (2R)-DOTAP chloride according to one or more of claims 1 to 4 in the manufacture of a cell transfecting medicament for the treatment of cancer.