Specification

Title of the Invention: Salt of 1-(2-deoxy-2-fluoro-4-thio-β-D-arabinofuranosyl)cytosine

Technical Field

[0001]

The present invention relates to a salt of 1-(2-deoxy-2-fluoro-4-thio-β-D-arabinofuranosyl)cytosine, which is useful as an antitumor agent.

Background Art

[0002]

It is known that 1-(2-deoxy-2-fluoro-4-thio-β-D-arabinofuranosyl)cytosine (henceforth also referred to as "Compound A") has superior antitumor activity, and is useful as a therapeutic agent for tumors (Patent document 1). It is also known that Compound A shows potent antitumor activity even when it is orally administered to mice (Non-patent documents 1 and 2).

Prior art references

Patent document

[0003]

Patent document 1: International Patent Publication WO97/038001

Non-patent documents

[0004]

Non-patent document 1: Cancer Letters, Vol. 144, pp.177-182, 1999

Non-patent document 2: Oncology Reports, Vol. 9, pp.1319-1322, 2002

Summary of the Invention

Object to be Achieved by the Invention

[0005]

Compound A suffers from low water solubility, and therefore it is necessary to improve the solubility for use as a medicament for humans. Compound A also suffers from poor flowability and tableting property, and therefore it has a problem concerning pharmaceutical manufacturing using it.

Thus, there is highly desired Compound A showing high water solubility, superior storage stability, flowability, and/or tableting property.

Summary

[0005a]
In one aspect of the present disclosure, there is provided a method for preparing a crystal of methanesulfonate of 1-(2-deoxy-2-fluoro-4-thio-β-D-arabinofuranosyl)cytosine showing characteristic peaks at diffraction angles (2θ) of 19.8, 21.8, 27.5, 28.4, and 29.9 degrees in powder X-ray diffractometry, which comprises the step of converting 1-(2-deoxy-2-fluoro-4-thio-β-D-arabinofuranosyl)cytosine into the methanesulfonate thereof and crystallizing said salt.
[0005b]
In another aspect of the present disclosure, there is provided a use of a crystal of methanesulfonate of 1-(2-deoxy-2-fluoro-4-thio-β-D-arabinofuranosyl)cytosine showing characteristic peaks at diffraction angles (2θ) of 19.8, 21.8, 27.5, 28.4, and 29.9 degrees in powder X-ray diffractometry, in the manufacture of a medicament for treating a tumor in a subject.
[0005c]
In a further aspect of the present disclosure, there is provided a crystal of hydrochloride of 1-(2-deoxy-2-fluoro-4-thio-β-D-arabinofuranosyl)cytosine showing characteristic peaks at diffraction angles (2θ) of 9.2, 14.7, 15.7, 22.9, and 27.3 degrees in powder X-ray diffractometry.
[0005d]
In another aspect of the present disclosure, there is provided a pharmaceutical composition containing the crystal defined herein and a pharmaceutically acceptable additive.
[0005e]
In a further aspect of the present disclosure, there is provided a pharmaceutical composition defined herein, which is for use in a treatment of a tumor.
[0005f]
In another aspect of the present disclosure, there is provided a method for preparing the crystal defined herein, which comprises the step of converting 1-(2-deoxy-2-fluoro-4-thio-β-D-arabinofuranosyl)cytosine into the hydrochloride thereof and crystallizing said salt.

[0005g]

In a further aspect of the present disclosure, there is provided a use of the crystal defined herein, in the manufacture of a medicament for treating a tumor in a subject.

Means for Achieving the Object

[0006]

The inventors of the present invention conducted various researches under such

Claims

1. A method for preparing a crystal of methanesulfonate of 1-(2-deoxy-2-fluoro-4-thio-β-D-arabinofuranosyl)cytosine showing characteristic peaks at diffraction angles (2θ) of 19.8, 21.8, 27.5, 28.4, and 29.9 degrees in powder X-ray diffractometry, which comprises the step of converting 1-(2-deoxy-2-fluoro-4-thio-β-D-arabinofuranosyl)cytosine into the methanesulfonate thereof and crystallizing said salt.

2. Use of a crystal of methanesulfonate of 1-(2-deoxy-2-fluoro-4-thio-β-D-arabinofuranosyl)cytosine showing characteristic peaks at diffraction angles (2θ) of 19.8, 21.8, 27.5, 28.4, and 29.9 degrees in powder X-ray diffractometry, in the manufacture of a medicament for treating a tumor in a subject.

3. A crystal of hydrochloride of 1-(2-deoxy-2-fluoro-4-thio-β-D-arabinofuranosyl)cytosine showing characteristic peaks at diffraction angles (2θ) of 9.2, 14.7, 15.7, 22.9, and 27.3 degrees in powder X-ray diffractometry.

4. A pharmaceutical composition containing the crystal according to claim 3 and a pharmaceutically acceptable additive.

5. The pharmaceutical composition according to claim 4, which is for use in a treatment of a tumor.

6. A method for preparing the crystal according to claim 3, which comprises the step of converting 1-(2-deoxy-2-fluoro-4-thio-β-D-arabinofuranosyl)cytosine into the hydrochloride thereof and crystallizing said salt.

7. Use of the crystal according to claim 3, in the manufacture of a medicament for treating a tumor in a subject.