POLYMORPHIC, CRYSTALLINE AND MESOPHASE FORMS OF SODIUM 2-(5-BROMO-4-(4-CYCLOPROPYLNAPHTHALEN-1-YL)-4*H*-1,2,4-TRIAZOL-3-YLTHIO)ACETATE, AND USES THEREOF

CROSS REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 61/293,602, filed January 8, 2010 which is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

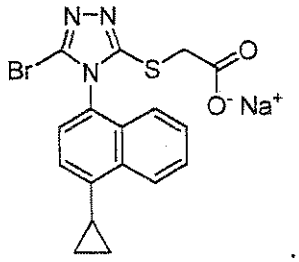
[0002] The present invention relates to polymorphic, crystalline and mesophase forms of sodium 2-(5-bromo-4-(4-cyclopropylnaphthalen-1-yl)-4H-1,2,4-triazol-3-ylthio)acetate, which decreases uric acid levels.

BACKGROUND OF THE INVENTION

[0003] Gout is associated with elevated levels of uric acid that crystallize and deposit in joints, tendons, and surrounding tissues. Gout is marked by recurrent attacks of red, tender, hot, and/or swollen joints.

SUMMARY OF THE DISCLOSUREINVENTION

[0004] Described herein are crystal polymorphs, mesophases, and other forms of sodium 2-(5-bromo-4-(4-cyclopropylnaphthalen-1-yl)-4*H*-1,2,4-triazol-3-ylthio)acetate:



[0005] One aspect described herein are crystalline polymorphs of sodium 2-(5-bromo-4-(4-cyclopropylnaphthalen-1-yl)-4*H*-1,2,4-triazol-3-ylthio)acetate characterized by peaks at 4.90, 9.83, and 25.29 °2θ±0.1°2θ. In further embodiment, such a crystalline polymorph is further characterized by at least two further peaks at 6.86, 8.41, 10.13, 17.92, and 23.10 °2θ±0.1°2θ. In yet still further embodiments, the crystalline polymorph exhibits an x-ray powder diffraction pattern substantially the same as the x-ray powder diffraction pattern shown in FIGURE 1. In a related aspect described herein are crystalline polymorphs of sodium 2-(5-bromo-4-(4-cyclopropylnaphthalen-1-yl)-4*H*-1,2,4-triazol-3-ylthio)acetate,

forms of sodium 2-(5-bromo-4-(4-cyclopropylnaphthalen-1-yl)-4*H*-1,2,4-triazol-3-ylthio)acetate; and at least one excipient or carrier.

[0013] In a further aspect are methods for treating or preventing hyperuricemia or a disease caused by elevated uric acid levels, comprising administering an effective amount of at least two of the aforementioned crystalline polymorph or solid mesophase forms of sodium 2-(5-bromo-4-(4-cyclopropylnaphthalen-1-yl)-4*H*-1,2,4-triazol-3-ylthio)acetate; and at least one excipient or carrier.

[0013a] In a first aspect, there is provided the use of an effective amount of the crystalline polymorph as defined herein, in the manufacture of a medicament for treating or preventing hyperuricemia, or a disease caused by elevated uric acid levels.

[0013b] In a second aspect, there is provided the use of an effective amount of at least two of the forms of sodium 2-(5-bromo-4-(4-cyclopropylnaphthalen-1-yl)-4*H*-1,2,4-triazol-3-ylthio)acetate selected from the group consisting of: the crystalline polymorph as defined herein as an active ingredient and the solid mesophase as defined herein as an active ingredient; and at least one excipient or carrier, in the manufacture of a medicament for treating or preventing hyperuricemia, or a disease caused by elevated uric acid levels.

[0013c] In a third aspect, there is provided the use of an effective amount of the crystalline polymorph as defined herein, in the manufacture of a medicament for treating or preventing gout.

[0013d] In a fourth aspect, there is provided the use of an effective amount of at least two of the forms of sodium 2-(5-bromo-4-(4-cyclopropylnaphthalen-1-yl)-4*H*-1,2,4-triazol-3-ylthio)acetate selected from the group consisting of: the crystalline polymorph as defined herein as an active ingredient and the solid mesophase as defined herein as an active ingredient; and at least one excipient or carrier, in the manufacture of a medicament for treating or preventing gout.

[0013e] In a fifth aspect, there is provided a method for preparing a crystalline polymorph of sodium 2-(5-bromo-4-(4-cyclopropylnaphthalen-1-yl)-4*H*-1,2,4-triazol-3-ylthio)acetate comprising: a) contacting amorphous sodium 2-(5-bromo-4-(4-cyclopropylnaphthalen-1-yl)-4*H*-1,2,4-triazol-3-ylthio)acetate with water and an aprotic solvent; and b) isolating the solids from the mixture prepared in a step a).

INCORPORATION BY REFERENCE

[0014] All publications and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings.

[0016] FIGURE 1 represents an illustrative X-ray Powder Diffraction Pattern of Polymorph Form A.

[0017] FIGURE 2 represents an illustrative Differential Scanning Calorimetry pattern of Polymorph Form A.

[0018] FIGURE 3 represents an illustrative infrared spectrum of Polymorph Form A.

[0019] FIGURE 4 represents an illustrative Raman spectrum of Polymorph Form A.

[0020] FIGURE 5 represents an illustrative X-ray Powder Diffraction Pattern of Polymorph Form B.

[0021] FIGURE 6 represents an illustrative Differential Scanning Calorimetry pattern of Polymorph Form B.

[0022] FIGURE 7 represents an illustrative X-ray Powder Diffraction Pattern of Polymorph Form B'.

[0023] FIGURE 8 represents an illustrative Differential Scanning Calorimetry pattern of Polymorph Form B'.