or a prophylactic agent for diseases associated with xanthine oxidase such as gout, hyperuricemia, tumor lysis syndrome, urinary calculi, hypertension, dyslipidemia, diabetes, cardiovascular diseases such as arteriosclerosis or heart failure, kidney diseases such as diabetic nephropathy, respiratory diseases such as chronic obstructive pulmonary diseases, inflammatory bowel diseases or autoimmune diseases.

[Solution to Problem]

As a result of earnest studies with the above object, the present inventors have found that 2-[4-(2,2-dimethylpropoxy)-3-(1H-1,2,3,4-tetrazol-1-yl)phenyl]-4-methyl-1,3-thiazole-5-carboxylic acid (hereinafter, also referred to as a compound (I)) can be crystallized and exists as at least one type of crystal polymorph.

That is, the present invention provides the following.

[1] A crystal form A of 2-[4-(2,2-dimethylpropoxy)-3-(1H-1,2,3,4-tetrazol-1-yl)phenyl]-4-methyl-1,3-thiazole-5-carboxylic acid;

[2] The crystal form A as described herein, wherein the crystal form A has characteristic peaks at diffraction angles of 2θ = 7.2°, 11.3°, 15.9°, 17.9°, 20.8°, 22.3°, 23.1°, 23.8°, 24.3° and 28.6° in its powder X-ray diffraction spectrum;

[3] The crystal form A as described herein, wherein its powder X-ray diffraction spectrum has a pattern shown in Fig. 1;

[4] The crystal form A as described herein, wherein its exothermic peak in thermogravimetry/differential thermal analysis is at 232°C;

[5] A pharmaceutical composition comprising the crystal form A as described herein and a pharmaceutically acceptable carrier;

[6] A xanthine oxidase inhibitor comprising the crystal form A

as described herein as an active ingredient; and

[7] A therapeutic or prophylactic agent for one or more diseases selected from the group consisting of gout, hyperuricemia, tumor lysis syndrome, urinary calculi, hypertension, dyslipidemia, diabetes, cardiovascular diseases, kidney diseases, respiratory diseases, inflammatory bowel diseases and autoimmune diseases, comprising the crystal form A as described herein as an active ingredient.

[Advantageous Effects of Invention]

The present invention provides crystals of an azole benzene derivative, which are useful as therapeutic or prophylactic agents for diseases associated with xanthine oxidase such as gout, hyperuricemia, tumor lysis syndrome, urinary calculi, hypertension, dyslipidemia, diabetes, cardiovascular diseases such as arteriosclerosis or heart failure, kidney diseases such as diabetic nephropathy, respiratory diseases such as chronic obstructive pulmonary diseases, inflammatory bowel diseases or autoimmune diseases. These crystals can be used as an active pharmaceutical ingredient for producing pharmaceutical agent.

[Brief Description of Drawings]

[Fig. 1] Fig. 1 is a powder X-ray diffraction spectrum of crystal form A.

[Description of Embodiments]

"Xanthine oxidase" is used both in a broad sense that it is an enzyme for catalyzing an oxidation reaction from hypoxanthine to xanthine and further to uric acid and in a narrow sense that it is an oxidase type xanthine oxidoreductase which is one of the enzymes that catalyze the same reaction. In the present invention, unless otherwise specified, "xanthine oxidase" is collectively

mg/kg and 1 mg/kg.

From the above results, it was shown that 2-[4-(2,2-dimethylpropoxy)-3-(1H-1,2,3,4-tetrazol-1-yl)phenyl]-4-methyl-1,3-thiazole-5-carboxylic acid has a potent hypouricemic effect.

[Reference Example 5]

Prolonged hypouricemic effect (Normal Rats)

2-[4-(2,2-dimethylpropoxy)-3-(1H-1,2,3,4-tetrazol-1-yl)phenyl]-4-methyl-1,3-thiazole-5-carboxylic acid was administered to Sprague-Dawley male rats in the same manner as in Reference Example 4. After the blood was collected from the tail vein 24 hours after administration, the plasma was separated. The level of uric acid in the blood was measured by an uricase method using an absorption spectrometer and a uric acid determination kit (L type Wako UA F: Wako Pure Chemical Industries, Ltd.). The percentage of hypouricemic effect was determined by the following expression:

Percentage of hypouricemic effect (%) = (Level of uric acid of the control animal - Level of uric acid of the test compound-administered animal) × 100 / Level of uric acid of the control animal.

2-[4-(2,2-dimethylpropoxy)-3-(1H-1,2,3,4-tetrazol-1-yl)phenyl]-4-methyl-1,3-thiazole-5-carboxylic acid showed a hypouricemic effect of 50% or more in a dose of 10 mg/kg and 40% or more in a dose of 3 mg/kg at 24 hours after administration.

From the above results, it was shown that 2-[4-(2,2-dimethylpropoxy)-3-(1H-1,2,3,4-tetrazol-1-yl)phenyl]-4-methyl-1,3-thiazole-5-carboxylic acid has a prolonged hypouricemic effect over a long period of time.

[Reference Example 6]

Hypouricemic effect (Hyperuricemic beagle dogs)

The hypouricemic effect of 2-[4-(2,2-dimethylpropoxy)-3-(1H-1,2,3,4-tetrazol-1-yl)phenyl]-4-methyl-1,3-thiazole-5-carboxylic acid in oxonic acid-induced hyperuricmic beagle dog was confirmed. A test

CLAIMS

[Claim 1] A crystal form A of 2-[4-(2,2-dimethylpropoxy)-3-(1H-1,2,3,4-tetrazol-1-yl)phenyl]-4-methyl-1,3-thiazole-5-carboxylic acid.

[Claim 2] The crystal form A according to Claim 1, wherein the crystal form A has characteristic peaks at diffraction angles of 2θ = 7.2°, 11.3°, 15.9°, 17.9°, 20.8°, 22.3°, 23.1°, 23.8°, 24.3° and 28.6° in its powder X-ray diffraction spectrum.

[Claim 3] The crystal form A according to Claim 1, wherein its powder X-ray diffraction spectrum has a pattern shown in Fig. 1.

[Claim 4] The crystal form A according to Claim 1, wherein its exothermic peak in thermogravimetry/differential thermal analysis is at 232°C.

[Claim 5] A pharmaceutical composition comprising the crystal form A according to any one of claims 1 to 4 and a pharmaceutically acceptable carrier.

[Claim 6] A xanthine oxidase inhibitor comprising the crystal form A according to any one of claims 1 to 4 as an active ingredient.

[Claim 7] A therapeutic or prophylactic agent for one or more diseases selected from the group consisting of gout, hyperuricemia, tumor lysis syndrome, urinary calculi, hypertension, dyslipidemia, diabetes, cardiovascular diseases, kidney diseases, respiratory diseases, inflammatory bowel diseases and autoimmune diseases, comprising the crystal form A according to any one of claims 1 to 4 as an active ingredient.