Non-Patent Literature 29: Kidney cycling - Use of drugs for chronic kidney disease - Stage 25, ACE inhibitor and angiotensin 2 receptor blockers, Yuichi Miyagawa, MVM, Vol. 30, No. 194, 2021 1.
Non-Patent Literature 30: Kidney cycling - Use of drugs for chronic kidney disease - Stage 26, Beraprost sodium, Yuichi Miyagawa, MVM, Vol. 30, No. 195, 2021 3.
Non-Patent Literature 31: Chakrabarti S, Syme H, Brown C, Elliott J, Histomorphometry of feline chronic kidney disease and correlation with markers of renal dysfunction, Veterinary pathology, 2013; 50(1): 147-155.
Non-Patent Literature 32: McLeland S, Cianciolo RE, Duncan C, Quimby J, A comparison of biochemical and histopathologic staging in cats with chronic kidney disease, Veterinary pathology, 2015; 52(3): 524-534.
Non-Patent Literature 33: Brown CA, Elliott J, Schmiedt CW, Brown SA, Chronic Kidney Disease in Aged Cats: Clinical Features, Morphology, and Proposed Pathogeneses, Vet. Pathol., 2016; 53(2): 309-326.
Non-Patent Literature 34: Goto Y, Yamaguchi S, Tamura M, et al., A prostacyclin analog prevents the regression of renal microvascular network by inhibiting mitochondria-dependent apoptosis in the kidney of rat progressive glomerulonephritis, Prostaglandins Other Lipid Mediat., 2014; 112: 16-26.
Non-Patent Literature 35: Fujita et al., Vascular Biology & Medicine, 2006, Vol. 7, p. 281.
Non-Patent Literature 36: Harley L, Langston C, Proteinuria in dogs and cats, Can. Vet. J., 2012; 53(6): 631-638.

Summary

Technical Problem

[0031]

An object of the present disclosure is to provide a therapeutic method for a cat with CKD to inhibit progression of CKD into IRIS stage 4 or kidney death of a cat or to improve the overall survival rate or the observed survival rate by administering a therapeutic agent comprising, as an active ingredient, a compound represented by the formula (I) to a specific cat with CKD.

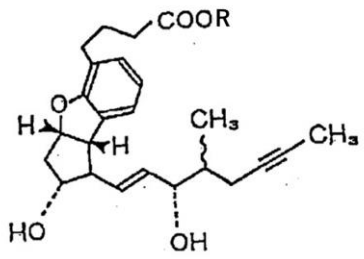
Solution to Problem

[0032]

Specifically, the present disclosure is as described below.

(1) A therapeutic method for a cat with CKD to inhibit progression of CKD into IRIS stage 4 or kidney death of a cat with CKD by administering a therapeutic agent comprising, as an active ingredient, a compound represented by the formula (I) to a cat with stage 3 or 4 CKD defined by the staging system established by the International Renal Interest Society (the IRIS staging) in an amount of 90 to 130 μg of the compound represented by the formula (I) daily:

[Formula 1]

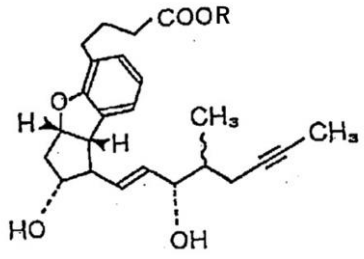


... (I)

wherein R represents hydrogen or a pharmacologically acceptable cation.

(2) A therapeutic method for a cat with CKD to improve the overall survival rate or the observed survival rate of a cat with CKD by administering a therapeutic agent comprising, as an active ingredient, a compound represented by the formula (I) to a cat with stage 3 or 4 CKD defined by the staging system established by the International Renal Interest Society (the IRIS staging) in an amount of 90 to 130 μg of the compound represented by the formula (I) daily:

[Formula 2]



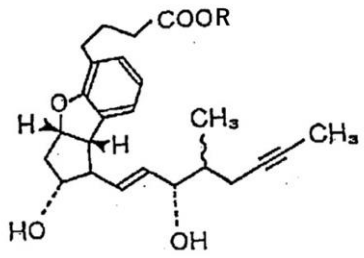
... (I)

wherein R represents hydrogen or a pharmacologically acceptable cation.

(3) The therapeutic method according to (1) or (2), wherein the compound represented by the formula (I) is beraprost sodium.

[0032a]

In one aspect, the present disclosure provides use of a compound represented by the formula (I):



... (I)

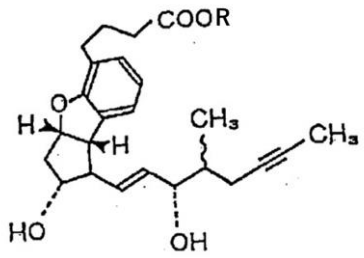
wherein R represents hydrogen or a pharmacologically acceptable cation,

in the manufacture of a medicament for treating a cat with chronic kidney disease, comprising, as an active ingredient, the compound represented by the formula (I),

wherein the medicament is to be administered to a cat with stage 4 chronic kidney disease defined by the staging system established by the International Renal Interest Society (the IRIS staging) in an amount of 90 to 130 μg of the compound represented by the formula (I) daily to inhibit kidney death of the cat.

[0032b]

In another aspect, the present disclosure provides use of a compound represented by the formula (I):



... (I)

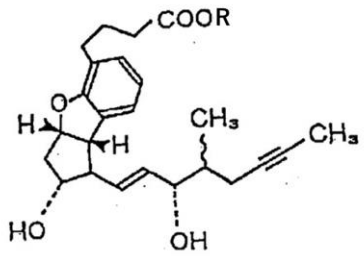
wherein R represents hydrogen or a pharmacologically acceptable cation,

in the manufacture of a medicament for treating a cat with chronic kidney disease, comprising, as an active ingredient, the compound represented by the formula (I),

wherein the medicament is to be administered to a cat with stage 4 chronic kidney disease defined by the staging system established by the International Renal Interest Society (the IRIS staging) in an amount of 90 to 130 μg of the compound represented by the formula (I) daily to improve the overall survival rate or the observed survival rate of the cat.

[0032c]

In another aspect, the present disclosure provides use of a compound represented by the formula (I):



... (I)

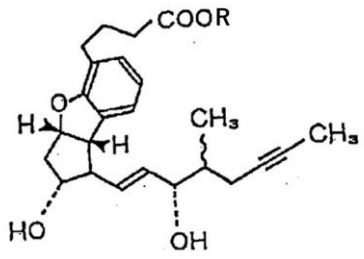
wherein R represents hydrogen or a pharmacologically acceptable cation,

in the manufacture of a medicament for treating a cat with chronic kidney disease, comprising, as an active ingredient, the compound represented by the formula (I),

wherein the medicament is to be administered to a cat with stage 3 chronic kidney disease defined by the staging system established by the International Renal Interest Society (the IRIS staging) in an amount of 90 to 130 μg of the compound represented by the formula (I) daily to improve the overall survival rate or the observed survival rate of the cat.

[0032d]

In another aspect, the present disclosure provides use of a compound represented by the formula (I):



... (I)

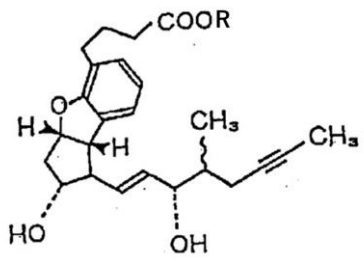
wherein R represents hydrogen or a pharmacologically acceptable cation,

in the manufacture of a medicament for treating a cat with chronic kidney disease, comprising, as an active ingredient, the compound represented by the formula (I),

wherein the medicament is to be administered to a cat with stage 3 chronic kidney disease defined by the staging system established by the International Renal Interest Society (the IRIS staging) having also complications/comorbidities such as chronic heart failure, diabetes mellitus, pancreatitis, neoplasia, hyperthyroidism, hypertension, proteinuria, hypokalemia, hyperphosphatemia, or anemia in an amount of 90 to 130 μg of the compound represented by the formula (I) daily to improve the overall survival rate or the observed survival rate of the cat.

[0032e]

In another aspect, the present disclosure provides use of a compound represented by the formula (I):



... (I)

wherein R represents hydrogen or a pharmacologically acceptable cation,

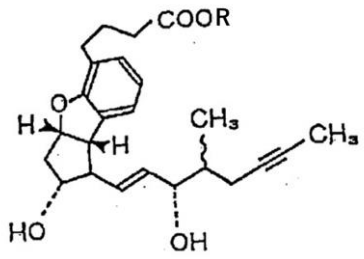
in the manufacture of a medicament for treating a cat with chronic kidney disease, comprising, as an active ingredient, the compound represented by the formula (I),

wherein the medicament is to be administered to a cat with stage 3 or 4 chronic kidney disease defined by the staging system established by the International Renal Interest Society (the IRIS staging) exhibiting body weight loss to less than 4.2 kg in an amount of 90 to 130 μg of the compound represented by the formula (I) daily to improve the overall survival rate or the observed survival rate of the cat.

CLAIMS

[Claim 1]

Use of a compound represented by the formula (I):



... (I)

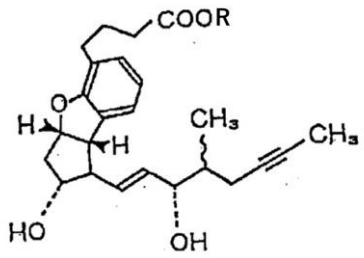
wherein R represents hydrogen or a pharmacologically acceptable cation,

in the manufacture of a medicament for treating a cat with chronic kidney disease, comprising, as an active ingredient, the compound represented by the formula (I),

wherein the medicament is to be administered to a cat with stage 4 chronic kidney disease defined by the staging system established by the International Renal Interest Society (the IRIS staging) in an amount of 90 to 130 μg of the compound represented by the formula (I) daily to inhibit kidney death of the cat.

[Claim 2]

Use of a compound represented by the formula (I):



... (I)

wherein R represents hydrogen or a pharmacologically acceptable cation,

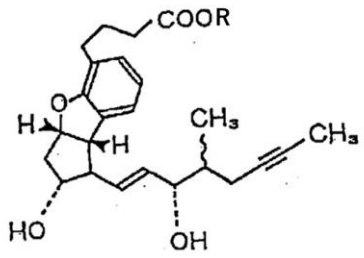
in the manufacture of a medicament for treating a cat with chronic kidney disease, comprising, as an active ingredient, the compound represented by the formula (I),

wherein the medicament is to be administered to a cat with stage 4 chronic kidney disease defined by the staging system established by the International Renal Interest Society (the IRIS staging) in an amount of 90 to 130 μg of the compound represented by the formula (I) daily to

improve the overall survival rate or the observed survival rate of the cat.

[Claim 3]

Use of a compound represented by the formula (I):



... (I)

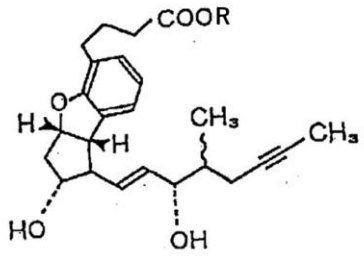
wherein R represents hydrogen or a pharmacologically acceptable cation,

in the manufacture of a medicament for treating a cat with chronic kidney disease, comprising, as an active ingredient, the compound represented by the formula (I),

wherein the medicament is to be administered to a cat with stage 3 chronic kidney disease defined by the staging system established by the International Renal Interest Society (the IRIS staging) in an amount of 90 to 130 μg of the compound represented by the formula (I) daily to improve the overall survival rate or the observed survival rate of the cat.

[Claim 4]

Use of a compound represented by the formula (I):



... (I)

wherein R represents hydrogen or a pharmacologically acceptable cation,

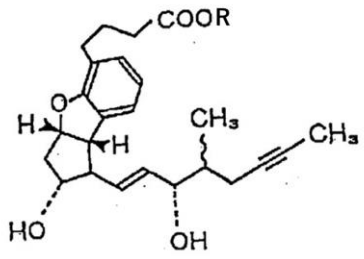
in the manufacture of a medicament for treating a cat with chronic kidney disease, comprising, as an active ingredient, the compound represented by the formula (I),

wherein the medicament is to be administered to a cat with stage 3 chronic kidney disease defined by the staging system established by the International Renal Interest Society (the IRIS staging) having also complications/comorbidities such as chronic heart failure, diabetes mellitus, pancreatitis, neoplasia, hyperthyroidism, hypertension, proteinuria, hypokalemia,

hyperphosphatemia, or anemia in an amount of 90 to 130 μg of the compound represented by the formula (I) daily to improve the overall survival rate or the observed survival rate of the cat.

[Claim 5]

Use of a compound represented by the formula (I):



... (I)

wherein R represents hydrogen or a pharmacologically acceptable cation,

in the manufacture of a medicament for treating a cat with chronic kidney disease, comprising, as an active ingredient, the compound represented by the formula (I),

wherein the medicament is to be administered to a cat with stage 3 or 4 chronic kidney disease defined by the staging system established by the International Renal Interest Society (the IRIS staging) exhibiting body weight loss to less than 4.2 kg in an amount of 90 to 130 μg of the compound represented by the formula (I) daily to improve the overall survival rate or the observed survival rate of the cat.

[Claim 6]

The use according to any one of claims 1 to 5, wherein the compound represented by the formula (I) is beraprost sodium.

[Claim 7]

The use according to any one of claims 1 to 4, wherein the cat having chronic kidney disease with IRIS stage 3 or 4 exhibits body weight loss to less than 4.2 kg.

[Claim 8]

The use according to any one of claims 3 to 5, wherein the cat having chronic kidney disease with IRIS stage 3 exhibits serum creatinine of 2.9 mg/dL to 5.0 mg/dL and serum SDMA of 9.0 μg/dL or higher.

[Claim 9]

The use according to any one of claims 1, 2 and 5, wherein the cat having chronic kidney disease with IRIS stage 4 exhibits serum creatinine of higher than 5.0 mg/dL and serum

SDMA of 9.0 μg/dL or higher.

[Claim 10]

The use according to claim 5, wherein the medicament is to be administered to the cat having chronic kidney disease with IRIS stage 3.

[Claim 11]

The use according to any one of claims 1 to 10, wherein the cat having chronic kidney disease with IRIS stage 3 or 4 satisfies the serum creatinine criterion of the IRIS staging criteria.

[Claim 12]

The use according to any one of claims 1 to 11, wherein the compound represented by the formula (I) is to be administered to the cat with chronic kidney disease in an amount of 14.1 to 52.4 μg/kg body weight/day.

[Claim 13]

The use according to any one of claims 1 to 12, wherein administration to the cat with chronic kidney disease is to be performed twice daily.

[Claim 14]

The use according to any one of claims 1 to 13, wherein administration to the cat with chronic kidney disease is to be performed during or after feeding.

[Claim 15]

The use according to any one of claims 1 to 14, wherein administration to the cat with chronic kidney disease is to be performed in addition to a standard care for feline chronic kidney disease.

[Claim 16]

The use according to claim 15, wherein the standard care is a therapeutic method defined by the guidelines from the International Society of Feline Medicine or the International Renal Interest Society.

[Claim 17]

The use according to any one of claims 1 to 3 and 5 to 16, wherein the cat with chronic kidney disease also has chronic heart failure, diabetes mellitus, pancreatitis, neoplasia, hyperthyroidism, hypertension, proteinuria, hypokalemia, hyperphosphatemia, or anemia.