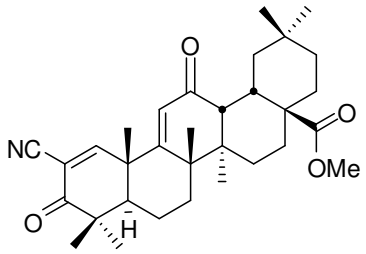
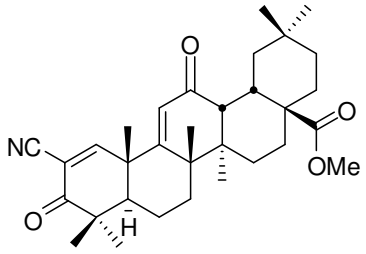
SUMMARY

In one aspect, the present invention refers to the use of a compound as shown by the following formula:



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or a pharmaceutically acceptable salt thereof in the preparation of a medicament for treating or preventing Alport syndrome in a patient. In another aspect, the present invention refers to the use of a compound as shown by the following formula:



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or a pharmaceutically acceptable salt thereof in the preparation of a medicament for improving kidney function of a patient who has been diagnosed with Alport syndrome. In one example, there are disclosed methods of treating or preventing Alport syndrome in a patients in need thereof, and/or improving the kidney function of patients who has been diagnosed with Alport syndrome. Such methods are described in the sections below, including for example the claims section, which is incorporated herein by reference.

In some examples, the compound is bardoxolone methyl (CDDO-Me or RTA 402). And in some of these examples, at least a portion of the CDDO-Me is present as a polymorphic form, wherein the polymorphic form is a crystalline form having an X-ray diffraction pattern (CuKα) comprising significant diffraction peaks at about 8.8, 12.9, 13.4, 14.2 and 17.4 °2θ. In non-limiting examples, the X-ray diffraction pattern (CuKα) is substantially as shown in FIG. 1A or FIG. 1B. In other variations, at least a portion of the CDDO-Me is present as a polymorphic form, wherein the polymorphic form is an amorphous form having an X-ray diffraction pattern (CuKα) with a halo peak at approximately 13.5 °2θ, substantially as shown in FIG. 1C, and a T_g. In some variations, the compound is an amorphous form. In some variations, the compound is a glassy solid form of CDDO-Me, having an X-ray powder diffraction pattern with a halo peak at about 13.5 °2θ, as shown in FIG. 1C, and a T_g. In some variations, the T_g value falls within a range of about 120 °C to about 135 °C. In some variations, the T_g value is from about 125 °C to about 130 °C.

In some examples, the compound is administered locally. In some examples, the compound is administered systemically. In some examples, the compound is administered orally, intraadiposally, intraarterially, intraarticularly, intracranially, intradermally, intralesionally, intramuscularly, intranasally, intraocularly, intrapericardially, intraperitoneally, intrapleurally, intraprostatically, intrarectally, intrathecally, intratracheally, intratumorally, intraumbilically, intravaginally, intravenously, intravesicularlly, intravitreally, liposomally, locally, mucosally, orally, parenterally, rectally, subconjunctivally, subcutaneously, sublingually, topically, transbuccally, transdermally, vaginally, in crèmes, in lipid compositions, via a catheter, via a lavage, via continuous infusion, via infusion, via inhalation, via injection, via local delivery, via localized perfusion, bathing target cells directly, or any combination thereof. For example, in some variations, the compound is administered intravenously, intra-arterially or orally. For example, in some variations, the compound is administered orally.

In some examples, the compound is formulated as a hard or soft capsule, a tablet, a syrup, a suspension, a solid dispersion, a wafer, or an elixir. In some variations, the soft capsule is a gelatin capsule. In variations, the compound is formulated as a solid dispersion. In some variations the hard capsule, soft capsule, tablet or wafer further comprises a protective coating. In some variations, the formulated compound comprises an agent that delays absorption. In some variations, the formulated compound further comprises an agent that enhances solubility or dispersibility. In some variations, the compound is dispersed in a liposome, an oil-in-water emulsion or a water-in-oil emulsion.

In some examples, the pharmaceutically effective amount is a daily dose from about 0.1 mg to about 500 mg of the compound. In some variations, the daily dose is from about 1 mg to about 300 mg of the compound. In some variations, the daily dose is from about 10 mg to about 200 mg of the compound. In some variations, the daily dose is about 25 mg of the compound. In other variations, the daily dose is about 75 mg of the compound. In still other variations, the daily dose is about 150 mg of the compound. In further variations, the daily dose is from about 0.1 mg to about 30 mg of the compound. In some variations, the daily dose is from about 0.5 mg to about 20 mg of the compound. In some variations, the daily dose is from about 1 mg to about 15 mg of the compound. In some variations, the daily dose is from about 1 mg to about 10 mg of the compound. In some variations, the daily dose is from about 1 mg to about 5 mg of the compound. In some variations, the daily dose is from about 2.5 mg to about 30 mg of the compound. In some variations, the daily dose is about 2.5 mg of the compound. In other variations, the daily dose is about 5 mg of the compound. In other variations, the daily dose is about 10 mg of the compound. In other variations, the daily dose is about 15 mg of the compound. In other variations, the daily dose is about 20 mg of the compound. In still other variations, the daily dose is about 30 mg of the compound.

In some examples, the pharmaceutically effective amount is a daily dose of 0.01 – 25 mg of compound per kg of body weight. In some variations, the daily dose is 0.05 – 20 mg of compound per kg of body weight. In some variations, the daily dose is 0.1 – 10 mg of compound per kg of body

weight. In some variations, the daily dose is 0.1 – 5 mg of compound per kg of body weight. In some variations, the daily dose is 0.1 – 2.5 mg of compound per kg of body weight.

In some examples, the pharmaceutically effective amount is administered in a single dose per day. In some examples, the pharmaceutically effective amount is administered in two or more doses per day.

In some examples, the patient is a mammal such as primate. In some variations, the primate is a human. In other variations, the patient is a cow, horse, dog, cat, pig, mouse, rat or guinea pig.

In some variations of the above methods, the compound is substantially free from optical isomers thereof. In some variations of the above methods, the compound is in the form of a pharmaceutically acceptable salt. In other variations of the above methods, the compound is not a salt.

In some examples, the compound is formulated as a pharmaceutical composition comprising (i) a therapeutically effective amount of the compound and (ii) an excipient selected from the group consisting of (A) a carbohydrate, carbohydrate derivative, or carbohydrate polymer, (B) a synthetic organic polymer, (C) an organic acid salt, (D) a protein, polypeptide, or peptide, and (E) a high molecular weight polysaccharide. In some variations, the excipient is a synthetic organic polymer. In some variations, the excipient is selected from the group consisting of a hydroxypropyl methyl cellulose, a poly[1-(2-oxo-1-pyrrolidinyl)ethylene] or copolymer thereof, and a methacrylic acid – methylmethacrylate copolymer. In some variations, the excipient is hydroxypropyl methyl cellulose phthalate ester. In some variations, the excipient is PVP/VA. In some variations, the excipient is a methacrylic acid – ethyl acrylate copolymer. In some variations, the methacrylic acid and ethyl acrylate may be present at a ratio of about 1:1. In some variations, the excipient is copovidone.

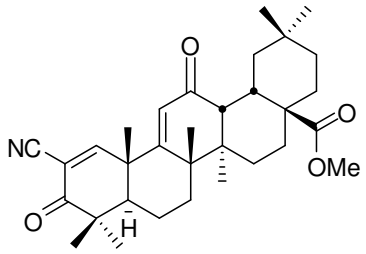
Any embodiment discussed herein with respect to one aspect of the invention applies to other aspects of the invention as well, unless specifically noted.

Further aspects and embodiments of this invention are elaborated in greater detail, for example, in the claims section, which is incorporated herein by reference.

Other objects, features and advantages of the present disclosure will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating specific embodiments of the invention, are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description. Note that simply because a particular compound is ascribed to one particular generic formula does not mean that it cannot also belong to another generic formula.

CLAIMS

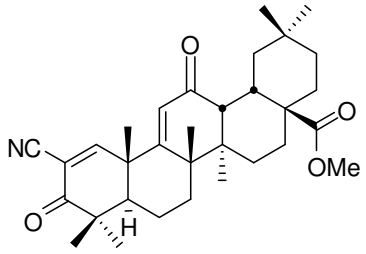
1. Use of a compound as shown by the following formula:



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or a pharmaceutically acceptable salt thereof in the preparation of a medicament for treating or preventing Alport syndrome in a patient.

2. Use of a compound as shown by the following formula:



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or a pharmaceutically acceptable salt thereof in the preparation of a medicament for improving kidney function of a patient who has been diagnosed with Alport syndrome.

3. The use medicament of claim 1 or 2, wherein the patient does not have cardiovascular disease.

4. The use of any one of claims 1 to 3, wherein the cardiovascular disease is left-sided myocardial disease, atherosclerosis, restenosis, thrombosis, or pulmonary hypertension.

5. The use of any one of claims 1 to 4, wherein the patient does not have Stage 4 or higher chronic kidney disease.

6. The use of any one of claims 1 to 4, wherein the patient does not have an estimated glomerular filtration rate (eGFR) less than 45 mL/min/1.73 m^2.

7. The use of any one of claims 1 to 4, wherein the patient does not have an elevated albumin/creatinine ratio (ACR) is greater than 2000 mg/g.

8. The use of any one of claims 1 to 7, wherein the patient does not have diabetes.

9. The use of any one of claims 1 to 7, wherein the patient does not have a complication associated with diabetes.

10. The use of any one of claims 1 to 9, wherein the patient does not have insulin resistance.

11. The use of any one of claims 1 to 10, wherein the patient does not have fatty liver disease.

12. The use of any one of claims 1 to 11, wherein the patient does not have hepatic impairment.

13. The use of any one of claims 1 to 12, wherein the patient is not overweight.

14. The use of any one of claims 1 to 13, wherein the patient does not have cancer.

15. The use of any one of claims 1 to 14, wherein the patient does not have chronic obstructive pulmonary disease (COPD).

16. The use of any one of claims 1 to 15, wherein the patient is not a smoker.

17. The use of any one of claims 1 and 3 to 16, wherein the patient has impaired renal function.

18. The use of any one of claims 1 to 17, wherein the patient has elevated levels of at least one biomarker associated with renal disease, which is selected from serum creatinine, cystatin C and uric acid.

19. The use of any one of claims 1 to 18, wherein the Alport syndrome is X-linked, autosomal recessive, or autosomal dominant.

20. The use of any one of claims 1 to 19, wherein the patient has a deletion or nonsense mutation of *COL4A5,* a splicing mutation of *COL4A5,* a missense mutation of *COL4A5,* a mutation in *COL4A3,* or a mutation in *COL4A4*.

21. The use of any one of claims 1 to 20, wherein the patient exhibits microhematuria.

22. The use of any one of claims 1 to 21, wherein the patient further exhibits microalbuminuria.

23. The use of any one of claims 1 to 22, wherein the patient further exhibits proteinuria.

24. The use of any one of claims 1 to 23, wherein the patient is less than 75 years old.

25. The use of any one of claims 1 to 24, wherein the patient does not have the following characteristics:

(A) a cardiovascular disease;

(B) an elevated baseline B-type natriuretic peptide (BNP) level;

(C) an estimated glomerular filtration rate (eGFR) < 45 mL/min/1.73 m^2; and

(D) an elevated albumin/creatinine ratio (ACR) > 2000 mg/g.

26. The use of any one of claims 1 to 25, wherein at least a portion of the compound is present as a crystalline form having an X-ray diffraction pattern (CuKα) comprising significant diffraction peaks at about 8.8, 12.9, 13.4, 14.2 and 17.4 °2θ.

27. The use of claim 26, wherein the X-ray diffraction pattern (CuKα) is substantially as shown in FIG. 1A or FIG. 1B.

28. The use of any one of claims 1 to 25, wherein at least a portion of the compound is present as an amorphous form having an X-ray diffraction pattern (CuKα) with a peak at approximately 13.5 °2θ, substantially as shown in FIG. 1C, and a transition glass temperature (T_g).

29. The use of claim 28, wherein the T_g value is in the range of about 120°C to about 135°C.

30. The use of claim 29, wherein the T_g value is in the range of about 125 C to about 130°C.

31. The use of any one of claims 1 to 30, wherein the compound is used in an amount from about 0.1 mg to about 300 mg of the compound or a pharmaceutically acceptable salt thereof per day.

32. The use of any one of claims 1 to 31, wherein the medicament is to be administered orally, intraarterially or intravenously.

33. The use of any one of claims 1 to 32, wherein the medicament is formulated as a hard or soft capsule or a tablet.

34. The use of any one of claims 1 to 32, wherein the medicament is formulated as a solid dispersion comprising (i) the compound and (ii) an excipient.

35. The use of claim 34, wherein the excipient is a methacrylic acid – ethyl acrylate copolymer.

36. The use of any one of claims 1 to 35, which is characterized in that the medicament is used in combination with a second drug.

37. The use of claim 36, wherein the second drug is an angiotensin-converting enzyme inhibitor, an angiotensin receptor blocker, or an aldosterone antagonist.

38. The use of claim 37, wherein the angiotensin-converting enzyme inhibitor is Ramipril, enalapril, Lisinopril, benazepril, fosinopril, quinapril, cilazapril, or trandolapril.

39. The use of claim 37, wherein the angiotensin receptor blocker is losartan, candesartan, irbesartan, telmisartan, or valsartan.

40. The use of claim 37, wherein the aldosterone antagonist is spironolactone.